

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Alker, Harold Examiner #: 7402 Date: 12-13
 Art Unit: 1644 Phone Number: 302-344-72 Serial Number: 11/15/81
 Mail Box and Bldg Room Location: 9E12/1128 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic and describe as specifically as possible the subject matter to be searched.
 Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or
 utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if
 known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the
 appropriate serial number.

Jan,
Please search claims 1-3 in 11/15/81
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es: 11/15/81

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This file contains CAS Registry Numbers for easy and accurate substance identification.

L35 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:656369 HCAPLUS
DN 137:197354
TI **Diagnostics, assay methods and amelioration of muscular
dystrophy symptoms**
IN **Kaufman, Stephen J.**
PA The Board of Trustees of the University of Illinois, USA
SO ECT Int. Appl., 53 pp.
CODEN: EIXXD2
DT Patent
LA English
IC ICM 301N033-68
ICS C12Q001-68; C12N005-00; C12N015-00; A61P021-00; A61K048-00
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 1, 3, 14
FAN.CNT 1

The present database provides coding, and sequences for the diagnosis, genetic therapy of certain muscular dystrophies, esp. muscular dystrophy resulting from a deficiency in dystrophin protein in a familial deficiency in dystrophin and Duchenne, and Becker and congenital, and the identification of patients, which increase expression in the alpha

.7 integrin. Expression of the **integrin** **.alpha.7** polypeptide in muscle cells results in better phys. condition in a patient or an animal lacking normal levels of **dystrophin** or **dystrophin** and **utrophin**. The present disclosure further provides immunol. and nucleic acid based methods for the **diagnosis** of **scapulooperoneal muscular dystrophy**, where there is a redn. in or absence of **.alpha.7A integrin** expression in muscle tissue samples and normal levels of **laminin-2** 4 in those same samples. The present disclosure further provides methods for identifying compns. which increase the expression of **.alpha.7 integrin** protein in muscle cells of **dystrophy** patients. Muscle biopsies from 5 patients with **scapulooperoneal muscular dystrophy** were analyzed for **integrin** expression using immunofluorescence and western blot analyses. There was a marked redn. or absence of the **.alpha.7.beta. integrin** in all 5 patients as compared with normal healthy controls. In contrast, the **.alpha.7.beta. integrin** was detected in the lining of the blood vessels. Using an anti-**.alpha.7A** polyclonal antibody, little or no fluorescence signal was detected in all the samples. The **.beta.1D integrin** expression was normal.

- ST **diagnosis treatment muscular dystrophy**
alpha7 integrin; scapulooperoneal
muscular dystrophy diagnosis alpha7
integrin muscle
- IT **Laminins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (2; **diagnostics** and assay methods and amelioration of
muscular dystrophy symptoms)
- IT **Laminins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (4; **diagnostics** and assay methods and amelioration of
muscular dystrophy symptoms)
- IT **Muscular dystrophy**
 (Duchenne; **diagnostics** and assay methods and
 amelioration of **muscular dystrophy symptoms**)
- IT **PCR (polymerase chain reaction)**
 (RT-PCR (reverse transcription-PCR); **diagnostics** and assay
 methods and amelioration of **muscular dystrophy**
symptoms)
- IT **Animal tissue**
 (anal. of; **diagnostics** and assay methods and amelioration of
muscular dystrophy symptoms)
- IT **Chimeric gene**
 RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
 (Biological study, unclassified); ANST (Analytical study); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (animal, with human **.alpha.7 integrin**
 regulatory sequence; **diagnostics** and assay methods and
 amelioration of **muscular dystrophy symptoms**)
- IT **Gene, animal**
 RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
 (Biological study, unclassified); ANST (Analytical study); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (chimeric, with human **.alpha.7 integrin**
 regulatory sequence; **diagnostics** and assay methods and
 amelioration of **muscular dystrophy symptoms**)
- IT **Animal**
 LNA sequences
Diagnosis
 Disease models
 Drug delivery systems
 Drug screening

- gene therapy
- genetic vectors
- genotyping method
- Human
- Immunoassay
 - Muscle**
 - Muscular dystrophy**
 - Nucleic acid hybridization
 - Perfusion
 - Plasmids
 - Samples
 - Southern blot hybridization
 - Viral vectors
 - (diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT Primers (nucleic acid)
- Reporter gene
 - RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT **Dystrophin**
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT High throughput **screening**
 - (drug; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT mRNA
 - RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (for integrin .alpha.7.beta.
 - 1; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT Gene, animal
 - RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (for integrin .alpha.7.beta.
 - 1; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT Proteins
 - RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (green fluorescent, reporter gene coding sequence for; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT Drug screening
 - (high throughput; diagnostics and assay methods and amelioration of muscular dystrophy symptoms)
- IT Immunoassay
 - immunoblotting; diagnostics and assay methods and amelioration of muscular dystrophy symptoms
- IT Immunoassay
 - immunofluorescence; diagnostics and assay methods and amelioration of muscular dystrophy symptoms
- IT Drug delivery systems
 - injections, i.m.; diagnostics and assay methods and amelioration of muscular dystrophy symptoms
- IT Drug delivery systems
 - injections, i.v.; diagnostics and assay methods and amelioration of muscular dystrophy symptoms

- IT CD antigens
 - Integrins**
 - RL: BEN (Biosynthetic preparation ; BSU (Biological study, unclassified ;
 PAR (Pharmacological activity ; THU (Therapeutic use ; BIOL (Biological
 study) ; PREP (Preparation ; USES (Uses)
 - integrin .alpha.7, .alpha.7BM2;**
 - diagnostics** and assay methods and amelioration of
muscular dystrophy symptoms)
- IT CD antigens
 - Integrins**
 - RL: ANT (Analyte) ; BSU (Biological study, unclassified) ; DGN (Diagnostic
 use) ; ANST (Analytical study) ; BIOL (Biological study) ; USES (Uses)
 - (integrin .alpha.7; diagnostics**
 - and assay methods and amelioration of muscular**
 - dystrophy symptoms)**
- IT Antibodies
 - RL: ARS (Analytical reagent use) ; DGN (Diagnostic use) ; ANST (Analytical
 study) ; BIOL (Biological study) ; USES (Uses)
 - (labeled, to .alpha.7.beta.1; diagnostics** and assay methods
and amelioration of muscular dystrophy symptoms)
- IT Antibodies
 - RL: ARS (Analytical reagent use) ; DGN (Diagnostic use) ; ANST (Analytical
 study ; BIOL (Biological study) ; USES (Uses)
 - (monoclonal; diagnostics** and assay methods and amelioration
of muscular dystrophy symptoms)
- IT **Animal tissue culture**
 - muscle, with reporter gene; diagnostics** and assay methods
and amelioration of muscular dystrophy symptoms)
- IT Gene, animal
 - RL: ARS (Analytical reagent use) ; BEN (Biosynthetic preparation) ; BSU
 (Biological study, unclassified) ; ANST (Analytical study) ; BIOL
 (Biological study) ; PREP (Preparation) ; USES (Uses)
 - (regulatory, for human .alpha.7 integrin**
 - gene in reporter construct; diagnostics** and assay methods and
amelioration of muscular dystrophy symptoms)
- IT Antigens
 - RL: ARS (Analytical reagent use) ; BEN (Biosynthetic preparation) ; BSU
 (Biological study, unclassified) ; ANST (Analytical study) ; BIOL
 (Biological study) ; PREP (Preparation) ; USES (Uses)
 - reporter gene coding sequence for tag; diagnostics** and assay
methods and amelioration of muscular dystrophy
 - symptoms)**
- IT Cell
 - reporter gene expression in; diagnostics** and assay methods
and amelioration of muscular dystrophy symptoms)
- IT **Muscular dystrophy**
 - (scapuloperoneal; diagnostics** and assay methods and
amelioration of muscular dystrophy symptoms)
- IT Cell
 - (stem, .alpha.7 integrin-expressing,**
 - treatment with; diagnostics** and assay methods and
amelioration of muscular dystrophy symptoms
- IT Antibodies
 - RL: ARS (Analytical reagent use ; DGN (Diagnostic use ; ANST (Analytical
 study ; BIOL (Biological study ; USES (Uses)
 - (to .alpha.7.beta.1; diagnostics** and assay methods and
amelioration of muscular dystrophy symptoms
- IT Mouse
 - transgenic; diagnostics** and assay methods and amelioration
of muscular dystrophy symptoms
- IT Proteins
 - RL: BSU (Biological study, unclassified ; BIOL (Biological study
 utrophins; **diagnostics** and assay methods and amelioration of

- muscular dystrophy symptoms
- IT Myoblast
 .alpha.7 integrin-expressing, treatment
 with; **diagnostics** and assay methods and amelioration of
 muscular dystrophy symptoms
- IT Integrins
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic
 use); ANST (Analytical study); BIOL (Biological study); USES (Uses
 (.alpha.7A; **diagnostics** and assay methods
 and amelioration of **muscular dystrophy** symptoms)
- IT Integrins
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic
 use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (.alpha.7.beta.1;
diagnostics and assay methods and amelioration of
muscular dystrophy symptoms)
- IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 .beta.1; **diagnostics** and assay methods
 and amelioration of **muscular dystrophy** symptoms)
- IT 452103-13-7 452103-34-8
 RL: AFG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties);
 ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (nucleotide sequence RT-PCR primer; **diagnostics** and assay
 methods and amelioration of **muscular dystrophy**
 symptoms)
- IT 453615-67-3P
 RL: AFG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
 (Biological study, unclassified); PRP (Properties); ANST (Analytical
 study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence, reporter construct contg.; **diagnostics**
 and assay methods and amelioration of **muscular**
dystrophy symptoms)
- IT 9001-45-0P, .beta.-Glucuronidase 9014-00-3P, Luciferase 9031-11-2P,
 .beta.-Galactosidase 9073-60-3P, .beta.-Lactamase
 FL: AFG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
 (Biological study, unclassified); ANST (Analytical study); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (reporter gene coding sequence for; **diagnostics** and assay
 methods and amelioration of **muscular dystrophy**
 symptoms)
- IT 453661-46-6 453661-47-7 453661-48-8
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; **diagnostics**, assay methods
 and amelioration of **muscular dystrophy** symptoms)
- 135 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
 AN 2002:017920 HCAPLUS
 DN 137:292866
 TI Integrin .alpha.7.beta.1
 in muscular dystrophy myopathy of unknown etiology
- AN Pegoraro, Elena; Cepollaro, Fulvio; Brandini, Paola; Marin, Alessandra;
 Fanin, Marina; Trevisan, Carlo P.; El-Messlemani, Abdul Hassin; Tarone,
 Guido; Engvall, Eva; Hoffman, Eric F.; Angelini, Corrado
 Neuromuscular Center, University of Padova, Padova, 35128, Italy
- CO American Journal of Pathology 2002, 158:2, 2135-2145
 SO WJEN: AJPAA; ISSN: 0002-9440
- EE American Society for Investigative Pathology
 IT Journal
 LA English
 CC 14-11 Mammalian Pathological Biochemistry
 Section cross-references : 3
 AB To investigate the role of integrin .alpha.7

in muscle pathol., we used a "candidate gene" approach in a large cohort of muscular dystrophy myopathy patients. Antibodies against the intracellular domain of the integrin .alpha.7A and .alpha.7B were used to stain muscle biopsies from 210 patients with muscular dystrophy myopathy of unknown etiol. Levels of .alpha.7A and .alpha.7B integrin were found to be decreased in 35 of 210 patients (approx.17%). In six of these patients no integrin .alpha.7B was detected. Screening for .alpha.7B mutation in 30 of 35 patients detected only one integrin .alpha.7 missense mutation (the mutation on the second allele was not found) in a patient presenting with a congenital muscular dystrophy-like phenotype. No integrin .alpha.7 gene mutations were identified in all of the other patients showing integrin .alpha.7 deficiency. In the process of mutation anal., we identified a novel integrin .alpha.7 isoform presenting 72-bp deletion. This isoform results from a partial deletion of exon 21 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position 2644 in integrin .alpha.7 cDNA. This spliced isoform is present in about 12% of the chromosomes studied. We conclude that secondary integrin .alpha.7 deficiency is rather common in muscular dystrophy/myopathy of unknown etiol., emphasizing the multiple mechanisms that may modulate integrin function and stability.

ST integrin isoform mutation muscular dystrophy myopathy

IT Gene, animal

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study)
(ITGA7; genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy myopathy of unknown etiol.)

IT Mutation

(deletion; genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy/myopathy of unknown etiol.)

IT Diagnosis

(genetic; genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy/myopathy of unknown etiol.)

IT Genotypes

Human

Muscular dystrophy

Phenotypes

(genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy myopathy of unknown etiol.)

IT mRNA

RL: BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study)

(integrin .alpha.7 .beta.1 gene; genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy myopathy of unknown etiol.)

IT Mutation

(missense; genetics study of integrin .alpha.7 .beta.1 in muscular dystrophy/myopathy of unknown etiol.)

IT Mutation

(splice site; genetics study of integrin .alpha.7 .beta.1 in muscular

dystrophy myopathy of unknown etiol.

II Integrins

SI: PSY Biological study, unclassified ; B101 Biological study
 .alpha.7A and .alpha.7B
 isoforms; genetics study of integrin .alpha.
 7.beta.1 in muscular
 dystrophy/myopathy of unknown etiol.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
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135 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 1998 ABC
 AN 1998052011 HCAPLUS
 IN 12943819
 II Mutations in the integrin .alpha.7 gene

- cause congenital myopathy
- AD Hayashi, Yukiko K.; Onod, Fan-Li; Engvall, Eva; Oyawa, Megumu; Matsuda, Shie; Hirabayashi, Shinichi; Yokoshi, Kenji; Cisker, Barry L.; Kramer, Randall H.; Kaufman, Stephen J.; Oyawa, Eijiro; Sato, Yu-Ichi; Nomaka, Ikuya; Tsukahara, Toshifumi; Wang, Jian-Chou; Hoffman, Eric P.; Arahata, Kiichi
- CS Department of Neuromuscular Research, National Center of Neurology and Psychiatry, National Institute of Neuroscience, Tokyo, 187-8502, Japan
- SO Nature Genetics (1998), 19(1), 94-97
- COFEN: NGENEC; ISSN: 1061-4036
- EB Nature America
- ET Journal
- LA English
- CC 3-1 (Biochemical Genetics)
- Section cross-reference(s): 14
- AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin .alpha.7.beta.1**. **Integrin .beta.1** is expressed throughout the body, while **integrin .alpha.7** is more muscle-specific. To address the role of **integrin .alpha.7** in human muscle disease, the authors detd. **integrin .alpha.7** protein expression in muscle biopsies from 117 patients with unclassified congenital myopathy and congenital **muscular dystrophy** by immunocytochem. The authors found three unrelated patients with **integrin .alpha.7** deficiency and normal laminin .alpha.2 chain expression. To det. if any of these three patients had mutations of the **integrin .alpha.7** gene, ITGA7, the authors cloned and sequenced the full-length human ITGA7 cDNA, and **screened** the patients for mutations. One patient had splice mutations on both alleles; one causing a 21-bp insertion in the conserved cysteine-rich region, and the other causing a 98-bp deletion. A second patient was a compd. heterozygote for the same 98-bp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of ITGA7 mRNA. Clin., these patients showed congenital myopathy with delayed motor milestones. These results demonstrate that mutations in ITGA7 are involved in a form of congenital myopathy.
- ST ITGA7 gene mutation **integrin alpha7** myopathy
- IT Gene, animal
- RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIL (Biological study)
- (ITGA7; mutations in **integrin .alpha.7** gene cause congenital myopathy)
- IT **Muscle, disease**
- (congenital; mutations in **integrin .alpha.7** gene cause congenital myopathy)
- IT Mutation
- deletion; mutations in **integrin .alpha.7** gene cause congenital myopathy)
- IT Mutation
- (insertion; mutations in **integrin .alpha.7** gene cause congenital myopathy)
- IT CD antigens
- CD antigens
- Integrins**
- Integrins**
- RL: BSU (Biological study, unclassified); BIL (Biological study)
- integrin .alpha.7**; mutations in **integrin .alpha.7** gene cause congenital myopathy
- IT Mutation
- splice site; mutations in **integrin .alpha.**

7 gene cause congenital myopathy?

RE.ONT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RESUME

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= d 136 all tot

L26 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 2101:22352 HCAPLUS

DN 164:365225

TI Enhanced expression of the .alpha.7.beta.

1 integrin reduces muscular dystrophy
and restores viability in dystrophic mice

AU Burkin, Dean J.; Wallace, Gregory Q.; Nicol, Kimberly J.; Kaufman, David
J.; Kaufman, Stephen J.

CS Department of Cell and Structural Biology, University of Illinois, Urbana,
IL, 61801, USA

SC Journal of Cell Biology (2001), 152(6), 1207-1216

CODEN: JOLBAS; ISSN: 0021-9525

PB Rockefeller University Press

BT Journal

LA English

BT 14-11 Mammalian Pathological Biochemistry.

AB Muscle fibers attach to laminin in the basal lamina using two distinct
mechanisms: the dystrophin glycoprotein complex and the
.alpha.7.beta.1 integrin.

Defects in these linkage systems result in Duchenne muscular
dystrophy DMD, .alpha.2 laminin congenital muscular
dystrophy, sarcoglycan-related muscular
dystrophy, and .alpha.7 integrin

congenital muscular dystrophy. Therefore, the mol.
continuity between the extracellular matrix and cell cytoskeleton is
essential for the structural and functional integrity of skeletal muscle.

To test whether the **.alpha.7.beta.1 integrin** can compensate for the absence of **dystrophin**, we expressed the rat **.alpha.7** chain in **mdx utr-/-** mice that lack both **dystrophin** and **utrophin**. These mice develop a severe **muscular dystrophy** highly akin to that in **DMD**, and they also die prematurely. Using the muscle creatine kinase promoter, expression of the **.alpha.7BEX2 integrin** chain was increased 2.0-2.3-fold in **mdx/utr-/-** mice. Concomitant with the increase in the **.alpha.7** chain, its heterodimeric partner, **.beta.1B**, was also increased in the transgenic animals. Transgenic expression of the **.alpha.7BEX2** chain in the **mdx/utr-/-** mice extended their longevity by threefold, reduced kyphosis and the development of muscle disease, and maintained mobility and the structure of the neuromuscular junction. Thus, bolstering **.alpha.7.beta.1**

integrin-mediated assocn. of muscle cells with the extracellular matrix alleviates many of the symptoms of disease obsd. in **mdx/utr-/-** mice and compensates for the absence of the **dystrophin**- and **utrophin**-mediated linkage systems. This suggests that enhanced expression of the **.alpha.7.beta.1**

integrin may provide a novel approach to treat **DMD** and other muscle diseases that arise due to defects in the **dystrophin** glycoprotein complex.

ST **integrin alpha7beta1** muscle viability Duchenne muscular dystrophy

IT Muscular dystrophy
(Duchenne; **.alpha.7.beta.1**
1 **integrin** increased expression reduces
muscular dystrophy and restores viability in
dystrophic mice)

IT CD antigens

Integrins

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(**integrin .alpha.7; .alpha.**

7.beta.1 integrin increased

expression reduces muscular dystrophy and restores viability in dystrophic mice)

IT Mouse

(**mdx/utr-/-; .alpha.7.beta.1**

integrin increased expression reduces muscular dystrophy and restores viability in dystrophic mice)

IT Proteins, specific or class

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(**utrophins; .alpha.7.beta.1**

integrin increased expression reduces muscular dystrophy and restores viability in dystrophic mice

IT Cytoskeleton

Disease models

Extracellular matrix

Muscle

Neuromuscular junction

.alpha.7.beta.1

integrin increased expression reduces muscular dystrophy and restores viability in dystrophic mice

IT Dystrophin

RL: ADV Adverse effect, including toxicity ; BOC Biological occurrence ; EPR Biological process ; BSU Biological study, unclassified ; BIOL Biological study ; OCCU Occurrence ; PROC Process

.alpha.7.beta.1

integrin increased expression reduces muscular

dystrophy and restores viability in dystrophic mice

17 Integrins

RE: BAC Biological activity or effector, except adverse ; BIC Biological occurrence ; BPR Biological process ; BSC Biological study, unclassified ; BICL Biological study ; BCC Occurrence ; BPC Process

.alpha.7.beta.1;

.alpha.7.beta.1 integrin

increased expression reduces muscular dystrophy and restores viability in dystrophic mice

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ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS
 AN 2000:897992 HCAPLUS
 CN 135:180306
 TI Transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin
 AU Viziariakis, Ioannis S.; Yap, Chung-Chen; Chen, YaoQi; Zieber, Barry L.; Tsiftoglou, Asterios S.; Kramer, Randall H.
 CS Departments of Stomatology and Anatomy, University of California at San Francisco, San Francisco, CA, 94143-0512, USA
 SO Archives of Biochemistry and Biophysics (2001), 385(1), 108-116
 CODEN: ABEIA4; ISSN: 0003-9861
 PB Academic Press
 DT Journal
 LA English
 CC 18-2 (Mammalian Biochemistry)
 Section cross-reference(s): 3, 6
 AB The laminin-binding **.alpha.7.beta.1 integrin** receptor is highly expressed by skeletal and cardiac muscles, and has been suggested to be a crucial mol. during myogenic cell migration and differentiation. Absence of **integrin .alpha.7** subunit contributes to a form of **muscular dystrophy in integrin .alpha.7** null mice, whereas specific mutations in the **.alpha.7** gene are associ. in humans with congenital myopathy. To examine in more detail the potential role of **integrin .alpha.7** in human-related muscular disorders, we cloned **.alpha.7** cDNA by RT-PCR from human skeletal muscle mRNA and then expressed the full-length human **integrin .alpha.7** cDNA by transfection in several cell lines including MCF-7, C3-7, and NIH3T3 cells. The isolated cDNA corresponds to the human **.alpha.7X2R** alternative splice form. Expression of human **.alpha.7** was further confirmed by transfection of chimeric human/mouse **.alpha.7** cDNA constructs. To demonstrate the functionality of expressed human **.alpha.7**, adhesion expts. with transfected MCF-7 cells have confirmed the specific binding of human **.alpha.7** to laminin. In addn., mouse polyclonal and monoclonal antibodies were generated against the extracellular domain of human **.alpha.7** and used to analyze by flow cytometry MCF-7 and NIH3T3 cells transfected with the full-length of human **.alpha.7** cDNA. These results show for the first time the exogenous expression of functional full-length human **.alpha.7** cDNA, as well as the development of monoclonal antibodies against the human **.alpha.7** extracellular domain. Antibodies developed will be useful for further anal. of human disorders involving **.alpha.7** dysfunction and facilitate isolation of muscle stem cells (satellite cells) and thereby expand the opportunities for genetically modified transplantation treatment of human disease. © 2001 Academic Press.

CT human **integrin alpha7** cDNA sequence; transfection
 carcinoma cell human **integrin alpha7** laminin
 IT Animal cell line
 MCF-7; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin
 IT RNA splicing

- alternative, of **.alpha.7**; transfection of MCF-7 carcinoma cells with human **integrin .alpha.**
7 cDNA promotes adhesion to laminin)
- IT Neoplasm
 (cell, **.alpha.7** expression in; transfection of MCF-7 carcinoma cells with human **integrin .alpha.**
7 cDNA promotes adhesion to laminin)
- IT cDNA sequences
 (for human **integrin .alpha.7** isoform;
 transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT CD antigens
Integrins
 RL: BPR (Biological process); BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study); PROC (Process)
 (integrin **.alpha.7**; transfection of MCF-7 carcinoma cells with human **integrin .alpha.**
7 cDNA promotes adhesion to laminin)
- IT Muscle, disease
 (model; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT Antibodies
 RL: BEN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
 (monoclonal, against human **.alpha.7** extracellular domain; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT Protein sequences
 (of human **integrin .alpha.7** isoform;
 transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT Cell adhesion
 Transformation, genetic
 (transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT Laminins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT 204786-84-9, **Integrin .alpha.-7** (human heart)
 RL: BPR (Biological process); BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study); PROC (Process)
 (amino acid sequence; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)
- IT 222253-34-1, GenBank AF072132
 RL: BSU (Biological study, unclassified); FRP (Properties); BIOL (Biological study)
 (nucleotide sequence; transfection of MCF-7 carcinoma cells with human **integrin .alpha.7** cDNA promotes adhesion to laminin)

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L36 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2000 ACS

AN 2000:255680 HCAPLUS

DN 111:57092

TI Laminin .alpha.4 and Integrin .alpha.6 Are Upregulated in Regenerating Ry/dy Skeletal Muscle: Comparative Expression of Laminin and Integrin Isoforms in Muscles Regenerating after Crush Injury

AU Stokin, Lydia M.; Maley, Maira A. L.; Mock, Helga; von der Mark, Helga; von der Mark, Klaus; Cadalbert, Laurence; Farosi, Stefanie; Davies, Marilyn J.; McGeachie, John K.; Grounds, Miranda D.

CS Interdisciplinary Center for Clinical Research (IZKF), University of Erlangen-Nuremberg, Germany

SO Experimental Cell Research (2000), 256(2), 500-514

OTEN: ECREAL; ISSN: 0014-4827

FB Academic Press

DT Journal

LA English

CC 14-11 (Mammalian Pathological Biochemistry)

AB The expression of laminin isoforms and laminin-binding integrin receptors known to occur in muscle was investigated during myogenic regeneration after crush injury. Comparisons were made between dystrophic (dys) Ry/dy mice, which have reduced laminin .alpha.4 expression, and their normal littermates. The overall distal pattern of regeneration after crush injury was similar in dy/dy and control muscle, but proceeded faster in dy/dy mice. In vitro studies revealed a greater yield of mononuclear cell. extd. from dy/dy muscle and a reduced proportion of desmin-pos. cells upon in vitro cultivation, reflecting the presence of inflammatory cells and "preactivated" myoblasts due to ongoing regenerative processes within the endogenous dystrophic lesions. Laminin .alpha.4 was not detectable in skeletal muscle. Laminin .alpha.4 was present in basement membranes of mature myofibers and newly formed

myotubes in control and dy/dy muscles, albeit weaker in dy/dy. Laminin .alpha.2-neg. myogenic cells were detected in dy/dy and control muscle, suggesting the involvement of other laminin .alpha. chains in early myogenic differentiation, such as laminin .alpha.4 and .alpha.5 which were both transiently expressed in basement membranes of newly formed myotubes of dy/dy and control mice. **Integrin .beta.1** was expressed on endothelial cells, muscle fibers, and peripheral nerves in uninjured muscle and broadened after crush injury to the interstitium where it occurred on myogenic and nonmyogenic cells. **Integrin .alpha.3** was not expressed in uninjured or regenerating muscle, while **integrin .alpha.6** was expressed mainly on endothelial cells and peripheral nerves in uninjured muscle. Upon crush injury **integrin .alpha.6** increased in the interstitium mainly on nonmyogenic cells, including infiltrating leukocytes, endothelial cells, and fibroblasts. In dy/dy muscle, **integrin .alpha.6** occurred on some newly formed myotubes. **Integrin .alpha.7** was expressed on muscle fibers at the myotendinous junction and showed weak and irregular expression on muscle fibers. After crush injury, **integrin .alpha.7** expression extended to the newly formed myotubes and some myoblasts. However, many myoblasts and newly formed myotubes were **integrin .alpha.7** neg. No marked difference was obsd. in **integrin .alpha.7** expression between dy/dy and control muscle, either uninjured or after crush injury. Only laminin .alpha.4 and **integrin .alpha.6** expression patterns were notably different between dy/dy and control muscle. Expression of both mols. was more extensive in dy/dy muscle, esp. in the interstitium of regenerating areas and on newly formed myotubes. In view of the faster myogenic regeneration obsd. in dy/dy mice, the data suggest that laminin .alpha.4 and **integrin .alpha.6** support myogenic regeneration. However, whether these accelerated myogenic effects are a direct consequence of the reduced laminin .alpha.2 expression in dy/dy mice, or an accentuation of the ongoing regenerative events in focal lesions in the muscle, requires further investigation. c) 2000 Academic Press.

ST laminin alpha4 **integrin alpha6 dystrophic** muscle
regeneration crush injury

IT Blood vessel

(endothelium; laminin .alpha.4 and **integrin .alpha.6** are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Muscle

(fiber; laminin .alpha.4 and **integrin .alpha.6** are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Leukocyte

inflammatory; laminin .alpha.4 and **integrin .alpha.6** are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)

IT Muscle, disease

injury; laminin .alpha.4 and **integrin .alpha.6** are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury

IT CD antigens

CD antigens

Integrins

Integrins

BI: B17 Biological occurrence ; B2V Biological study, unclassified ; B12 Biological study ; C20V Occurrence

integrin .alpha.7; laminin .alpha.4 and

integrin .alpha.6 are upregulated in regenerating dy/dy

- dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to
- IT **Muscular dystrophy**
Regeneration, animal
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury)
- IT **Basement membrane**
Cell differentiation
Fibroblast
Myoblast
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT Desmins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT **Muscle**
Muscle
Tendon
Tendon
(muscle-tendon junction; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT **Muscle**
(myotubule; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT Nerve
(peripheral; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT Laminins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
.alpha.4, .alpha.1, .alpha.2, .alpha.5 chains; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury)
- IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.alpha.3; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury in relation to)
- IT **Integrins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
.alpha.6; laminin .alpha.4 and **integrin** .alpha.6 are upregulated in regenerating dy/dy **dystrophic** skeletal muscle (with reduced laminin .alpha.2 expression) after crush injury)
- IT **Integrins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

.beta.1; laminin .alpha.4 and integrin .alpha.6 are upregulated in regenerating myoblasts by dystrophic skeletal muscle with reduced laminin .alpha.4 expression after crush injury in relation to

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196 Nat, 3; J Cell Sci 1996, 109, 1139 HCARLUS

196 ANSWER 4 OF 11 HCARLUS COPYRIGHT 2013 ACS

AN 1311:84481 HCARLUS

DN 131:250000

TI Organization of the myotendinous junction is dependent on the presence of .alpha.7.beta.1 integrin

AU Miosge, Nicolai; Klenozar, Christina; Herken, Rainer; Willem, Michael; Mayer, Ulrike

CS Centrum Anatomie, Martinsried, 82152, Germany

SO Laboratory Investigation (1999), 79(12), 1591-1599

CO (CODEN: LAINAH; ISSN: 0023-6887)

PS Lippincott Williams & Wilkins

ST Journal

LA English

CC 13-1 (Mammalian Biochemistry)

AB The laminin receptor .alpha.7.beta.1 is enriched at the myotendinous junctions, and mice with a targeted inactivation of the .alpha.7 gene develop a form of muscular dystrophy that primarily affects this structure. By ultrastructural anal. of .alpha.7-deficient mice, in comparison with wild-type and mdx mice, we attempted to elucidate the role of .alpha.7 integrin for the integrity and function of the myotendinous junctions. Ultrastructurally, myotendinous junctions of .alpha.7-deficient myofibers lose their interdigitations and the myofilaments retract from the sarcolemmal membrane, whereas the lateral side of the myofibers remains morphol. normal. The basement membrane at the myotendinous junctions in .alpha.7 -/- mice is significantly broadened, and immunogold-histochem. has demonstrated that the laminin .alpha.2 chain is not localized here but, instead, in the matrix of the neighboring tendon. In contrast, mdx mice have normal myotendinous junctions, with a matrix protein pattern also found in wild-type mice; however, the lateral sides of the myofibers are severely damaged. These results suggest that the .alpha.7.beta.1 integrin is a major receptor connecting the muscle cell to the tendon and helps to organize the myotendinous junction, whereas the dystrophin-glycoprotein complex is necessary for the lateral integrity of the muscle cell.

ST myotendinous junction basement membrane laminin nidogen integrin alpha7 beta1

IT Muscle

(fiber; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.7.beta.1 integrin)

IT CD antigens

CD antigens

Integrins

Integrins

RL: BPR (Biological process; BSU (Biological study, unclassified); BIL (Biological study; PROC (Process

integrin .alpha.7; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.7.beta.1 integrin

IT Muscle

Muscle

Tendon

Tendon

muscle-tendon junction; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.7.beta.1 integrin

- IT Organelle
myofilament; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.
7.beta.1 integrin
- IT Entactin
RL: BOC (Biological occurrence); BSU Biological study, unclassified;
BIOL (Biological study); OCCU Occurrence
(nidogen, 1; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.
7.beta.1 integrin)
- IT Basement membrane
Tendon
organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.7
.beta.1 integrin)
- IT Cell membrane
sarcolemma; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.
7.beta.1 integrin
- IT Laminins
RL: BOC (Biological occurrence); BSU Biological study, unclassified;
BIOL (Biological study); OCCU Occurrence
(.alpha.2 chain; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.
7.beta.1 integrin)
- IT Integrins
FL: BIR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.7.beta.1; organization of mouse myotendinous junction and protein expression pattern is dependent on presence of .alpha.7.beta.
1 integrin)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
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136 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:637728 HCAPLUS

DN 131:335367

TI Activation of c-Raf-1 kinase signal transduction pathway in **.alpha.7 integrin**-deficient mice

AU Saher, Gesine; Hildt, Eberhard

CS Max-Planck-Institut fur Biochemie, Martinsried, D-82152, Germany

SO Journal of Biological Chemistry (1999), 274(39), 27651-27657

CODEN: JBCHA3; ISSN: 0021-9253

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 14-11 (Mammalian Pathological Biochemistry)

AB **Integrin .alpha.7**-deficient mice develop a novel form of **muscular dystrophy**. Here we report that deficiency of **.alpha.7 integrin** causes an activation of the c-Raf-1/mitogen-activated protein (MAP) 2 kinase signal transduction pathway in muscle cells. The obsd. activation of c-Raf-1/MAP2 kinases is a specific effect, because the **.alpha.7 integrin** deficiency does not cause unspecific stress as detd. by measurement of the Hsp72/73 level and activity of the JNK2 kinase. Because an increased level of activated FAK was found in muscle of **.alpha.7 integrin**-deficient mice, the activation of c-Raf-1 kinase is triggered most likely by an **integrin**-dependent pathway. In accordance with this, in the **integrin .alpha.7**-deficient mice, part of the **integrin .beta.1d** variant in muscle is replaced by the **.beta.1a** variant, which permits the FAK activation. A recent report describes that **integrin** activity can be down-modulated by the c-Raf-1/MAP2 kinase pathway. Specific activation of the c-Raf-1/MAP2 kinases by cell-permeable peptides in skeletal muscle of rabbits causes degeneration of muscle fibers. Therefore, we conclude that in **.alpha.7 integrin**-deficient mice, the continuous activation of c-Raf-1 kinase causes a permanent redn. of **integrin** activity diminishing **integrin**-dependent cell-matrix interactions and thereby contributing to the development of the **dystrophic** phenotype.

BT cRaf1 kinase signal transduction **integrin** deficiency muscle **dystrophy**

IT Proteins, specific or class

PT BPR: Biological process ; BSC: Biological study, unclassified ; BTL: Biological study ; BPOC: Process

[PreC1:PreC2; **.alpha.7 integrin**

deficiency causes an activation of c-Raf-1 mitogen-activated protein kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**

IT Muscle, disease

degeneration; **.alpha.7 integrin**

deficiency causes an activation of c-Raf-1 mitogen-activated protein ..

- kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**
- IT 00 Antigenes
00 Antigenes
Integrins
Integrins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**integrin .alpha.7; .alpha.7**
integrin deficiency causes an activation of
c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p125FAK; **.alpha.7 integrin** deficiency
causes an activation of c-Raf-1/mitogen-activated protein 2 kinase
signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT Disease models
Mouse
Muscle
Muscular dystrophy
Signal transduction, biological
(**.alpha.7 integrin** deficiency causes an
activation of c-Raf-1/mitogen-activated protein 2 kinase signal
transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.beta.1; .alpha.7**
integrin deficiency causes an activation of
c-Raf-1/mitogen-activated protein 2 kinase signal transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT 139691-76-2, c-Raf-1 kinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.alpha.7 integrin** deficiency causes an
activation of c-Raf-1/mitogen-activated protein 2 kinase signal
transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT 141467-21-2
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**.alpha.7 integrin** deficiency causes an
activation of c-Raf-1/mitogen-activated protein 2 kinase signal
transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
- IT 144114-16-2, Focal adhesion kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**.alpha.7 integrin** deficiency causes an
activation of c-Raf-1/mitogen-activated protein 2 kinase signal
transduction pathway in muscle cells in mouse model of **muscular dystrophy**)
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L36 ANSWER # OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 1996:196448 HCAPLUS

EN 111:71843

TI Laminin polymerization induces a receptor-cytoskeleton network

AU Colagato, Holly; Winkelmann, Donald A.; Yurchenco, Peter D.

CS Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Piscataway, NJ, 08854, USA

SO Journal of Cell Biology (1999), 145(3), 619-631

CODEN: JCLB49; ISSN: 0021-9525

PS Rockefeller University Press

DT Journal

LA English

CC 15-6 (Mammalian Biochemistry

Section cross-reference(s): 14

AB The transition of laminin from a monomeric to a polymeric state is thought to be a crucial step in the development of basement membranes and in the case of skeletal muscle, mutations in laminin can result in severe **muscular dystrophies** with basement membrane defects. We have evaluated laminin polymer and receptor interactions to determine the requirements for laminin assembly on a cell surface and investigated what cellular responses might be mediated by this transition. We found that on muscle cell surfaces, laminins preferentially polymerize while bound to receptors that included dystroglycan and **alpha.7. beta.1 integrin**. These receptor interactions are mediated through laminin COOH-terminal domains that are spatially and functionally distinct from NH2-terminal polymer binding sites. This receptor-facilitated self-assembly drives rearrangement of laminin into a cell-associated polygonal network, a process that also requires actin reorganization and tyrosine phosphorylation. As a result, dystroglycan and **integrin** redistribute into a reciprocal network as do cortical cytoskeleton components vinculin and **dystrophin**. Cytoskeletal and receptor reorganization is dependent on laminin polymerization and fails in response to receptor occupancy alone. Nonpolymeric laminin. Preferential polymerization of laminin on cell surfaces, and the resulting induction of cortical architecture, is a cooperative process requiring laminin-receptor ligation, receptor-facilitated self-assembly, actin reorganization, and signaling events.

ST Laminin polymer **integrin** dystroglycan cytoskeleton basement

- membrane muscular dystrophy
- IT **Muscular dystrophy**
 (implications of laminin polymn. induction of receptor-cytoskeleton network in)
- IT Actins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (laminin polymn. induces receptor-actin cytoskeleton network)
- IT Cytoskeleton
 Molecular association
 Polymerization
 (laminin polymn. induces receptor-cytoskeleton network)
- IT Laminins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (laminin polymn. induces receptor-cytoskeleton network)
- IT **Dystrophin**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (laminin polymn. induces receptor-cytoskeleton network contg.)
- IT Vinculin
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (laminin polymn. induces receptor-cytoskeleton network contg.)
- IT **Basement membrane**
Muscle
 (laminin polymn. induces receptor-cytoskeleton network in)
- IT **Muscle**
 myotubule; laminin polymn. induces receptor-cytoskeleton network in)
- IT Phosphorylation, biological
 protein; laminin polymn. induces receptor-cytoskeleton network involving tyrosine)
- IT Cell membrane
 sarcolemma; laminin polymn. induces receptor-cytoskeleton network on)
- IT Glycoproteins, specific class
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (.alpha.-dystroglycans; laminin polymn. induces receptor-cytoskeleton network contg.)
- IT **Integrins**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (.alpha.7.beta.1; laminin polymn. induces receptor-cytoskeleton network contg.)
- IT 60-16-4, L-Tyrosine, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (laminin polymn. induces receptor-cytoskeleton network involving phosphorylation of
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TI Secondary reduction of **.alpha.7B integrin** in
 laminin **.alpha.2** deficient congenital **muscular dystrophy**
 supports an additional transmembrane link in skeletal muscle
 AU Cohn, Ronald L.; Mayer, Ulrike; Saher, Gesine; Herrmann, Ralf; van der
 Elier, Arjan; Sonnenberg, Arnoud; Sorskin, Lydia; Voit, Thomas
 CS Departments of Pediatrics and Pediatric Neurology, University of Essen,
 Essen, 48122, Germany
 SO Journal of the Neurological Sciences (1999), 163(2), 143-152
 CODEN: JNSCAG; ISSN: 0302-510X
 PB Elsevier Science Ireland Ltd.
 DT Journal
 LA English
 CC 14-11 (Mammalian Pathological Biochemistry)
 AB The **integrins** are a large family of heterodimeric transmembrane
 cellular receptors which mediate the assocn. between the extracellular
 matrix (ECM) and cytoskeletal proteins. The **.alpha.7**
beta.1 integrin is a major laminin binding
integrin in skeletal and cardiac muscle and is thought to be
 involved in myogenic differentiation and migration processes. The main
 binding partners of the **.alpha.7 integrin**
 are laminin-1 (**.alpha.1-.beta.1-.gamma.1**), laminin-2
.alpha.2-.beta.1-.gamma.1) and laminin-4
.alpha.2-.beta.3-.gamma.1). Targeted deletion of the gene for the **.**
alpha.7 integrin subunit (**ITGA7**) in mice leads
 to a novel form of **muscular dystrophy**. In the present
 study we have investigated the expression of two alternative splice
 variants, the **.alpha.7B** and **.beta.1D integrin**
 subunits, in normal human skeletal muscle, as well as in various forms of
muscular dystrophy. In normal human skeletal muscle the
 expression of the **.alpha.7 integrin** subunit
 appeared to be developmentally regulated: it was first detected at 2 yr of
 age. In contrast, the **.beta.1D integrin** could be detected in
 immature and mature muscle in the sarcolemma of normal fetal skeletal
 muscle at 13 wk gestation. The expression of **.alpha.7B**
integrin was significantly reduced at the sarcolemma in six
 patients with laminin **.alpha.2** chain deficient congenital **muscular**
dystrophy (CMD) (age >2 yr). However, this redn. was not
 correlated with the amt. of laminin **.alpha.2** chain expressed. In
 contrast, the expression of the laminin **.alpha.2** chain was not altered in
 the skeletal muscle of the **.alpha.7** knock-out mice.
 These data arguing in favor that there is not a tight correlation between
 the expression of the **.alpha.7 integrin**
 subunit and that of the laminin **.alpha.2** chain in either human or murine
dystrophic muscle. Interestingly, in **dystrophinopathies**
 (Duchenne and Becker **muscular dystrophy**; DMD/BMD)
 expression of **.alpha.7B** was upregulated irresp. of the
 level of **dystrophin** expression as shown by a strong sarcolemmal
 staining pattern even in young boys (age <2 yr). The expression of the
.beta.1D integrin subunit was not altered in any of our patients
 with different types of **muscular dystrophy**. In
 contrast, sarcolemmal expression of **.beta.1D integrin** was
 significantly reduced in the **.alpha.7 integrin**
 knock-out mice, whereas the expression of the components of the **ECM** was
 not altered. The secondary loss of **.alpha.7B** in
 laminin **.alpha.2** chain deficiency defines a biochem. change in the compn.
 of the plasma membrane resulting from a primary protein deficiency in the
 basal lamina. These findings, in addn. to the occurrence of a
muscular dystrophy in **.alpha.7**
 deficient mice, implies that the **.alpha.7B**
integrin is an important laminin receptor within the plasma
 membrane which plays a significant role in skeletal muscle function and
 stability.

ST alpha7B integrin laminin alpha muscle

- dystrophy
- IT Muscular dystrophy
 Duchenne and Becker; secondary redn. of .alpha.
 7B integrin in laminin .alpha.2 deficient
 congenital muscular dystrophy skeletal
 muscle in humans and in mice
- IT Disease, animal
 (deficiency, laminin.alpha.2 chain; secondary redn. of .alpha.
 7B integrin in laminin .alpha.2 deficient congenital
 muscular dystrophy skeletal muscle in humans and in
 mice)
- IT Muscular dystrophy
 (laminin .alpha.2 chain deficient congenital; secondary redn.
 of .alpha.7B integrin in laminin .alpha.2
 deficient congenital muscular dystrophy
 skeletal muscle in humans and in mice)
- IT Cell membrane
 (sarcolemma; secondary redn. of .alpha.7B
 integrin in laminin .alpha.2 deficient congenital
 muscular dystrophy skeletal muscle in humans and in
 mice)
- IT Muscle
 (secondary redn. of .alpha.7B integrin in
 laminin .alpha.2 deficient congenital muscular
 dystrophy skeletal muscle in humans and in mice)
- IT Dystrophin
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BICL (Biological study); OCCU (Occurrence)
 (secondary redn. of .alpha.7B integrin in
 laminin .alpha.2 deficient congenital muscular
 dystrophy skeletal muscle in humans and in mice)
- IT Laminins
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BICL (Biological study); OCCU (Occurrence)
 (.alpha.2 chain deficiency; secondary redn. of .alpha.
 7B integrin in laminin .alpha.2 deficient congenital
 muscular dystrophy skeletal muscle in humans and in
 mice)
- IT Laminin receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.alpha.7B integrin is a; secondary redn.
 of .alpha.7B integrin in laminin .alpha.2
 deficient congenital muscular dystrophy skeletal
 muscle in humans and in mice)
- IT Integrins
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
 study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
 (Process)
 (.alpha.7B1; secondary redn. of .alpha.7B
 integrin in laminin .alpha.2 deficient congenital
 muscular dystrophy skeletal muscle in humans and in
 mice)
- IT Integrins
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BICL (Biological study); OCCU (Occurrence)
 (.beta.15; secondary redn. of .alpha.7B
 integrin in laminin .alpha.2 deficient congenital
 muscular dystrophy skeletal muscle in humans and in
 mice)
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45. Straub, V; J Cell Biol 1992, V119, P1163 HCAPLUS
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136 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACC

AN 1995:131122 HCAPLUS

IN 1995:127949

TI The .alpha.7.beta.1

integrin in muscle development and disease

AN Burklin, Jean P.; Kaufman, S. J.

DE Department of Cell and Structural Biology, University of Illinois, 617
Chemical and Life Sciences Laboratory, Urbana, IL, 61801, USA

JO Cell & Tissue Research 1995, 196:1, 195-197

ISBN: 0303-321X

EE Springer-Verlag

JJ Journal; General Review
 LA English
 CC 13-1 Mammalian Biochemistry
 Section cross-reference s: 14
 AB A review, with 43 refs. The **.alpha.7.beta.1 integrin** is a laminin receptor on the surface of skeletal myoblasts and myofibers. Alternative forms of both the **.alpha.7** and **.beta.1** chains are expressed in a developmentally regulated fashion during myogenesis. These different **.alpha.7.beta.1** isoforms localize at specific sites on myofibers and appear to have distinct functions in skeletal muscle. These functions include the migration and proliferation of developing myoblasts, the formation and integrity of neuromuscular and myotendinous junctions, and the "gluing" together of muscle fibers that is essential to the generation of contractile force. The **.alpha.7.beta.1 integrin** appears to be both directly and indirectly causally related to several muscle diseases. Enhanced expression of **.alpha.7.beta.1**-mediated linkage of the extracellular matrix is seen in Duchenne muscular dystrophy and may compensate for the absence of the dystrophin-mediated linkage. Downregulation of expression of the **integrin** may contribute to the development of pathol. in congenital laminin deficiencies. Mutations in the **.alpha.7** **integrin** gene underlie ainkl. congenital muscle diseases. The functional roles of this **integrin** in the formation and stability of the neuromuscular and myotendinous junctions and its localization between fibers suggest that altered expression or function of this **integrin** may have widespread involvement in other myopathies. The localization of the **.alpha.7** gene at human chromosome 12q13 is a useful clue for focusing such studies.
 ST review **integrin** muscle development disease
 IT Development, mammalian postnatal
 Muscle
 Muscle, disease
 (**.alpha.7.beta.1 integrin** in muscle development and disease)
 IT Integrins
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**.alpha.7.beta.1; .alpha.7.beta.1 integrin** in muscle development and disease)
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136 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:870188 HCAPLUS

DN 123:271470

TI The expression of the **alpha.7**beta(1)
 I **integrin** in skeletal muscle development and **muscular dystrophy**

AU Hodges, Bradley Lowell

CS Univ. of Illinois, Urbana, IL, USA

SO 1998; 107 pp. Avail.: UMI, Order No. DA9834690

From: Diss. Abstr. Int., E 1998, 59(5), 2030

DT Dissertation

LA English

CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 13, 14

AB Unavailable

ST **integrin** gene expression skeletal muscle development;
muscular dystrophy integrin expression

IT RNA splicing
 (alternative, **.alpha.7.beta.1**
integrin; expression of the **alpha(7)**
beta(1) integrin in skeletal muscle
 development and **muscular dystrophy**)

IT Muscle

Muscular dystrophy

expression of the **alpha.7 beta.1**

integrin in skeletal muscle development and
muscular dystrophy

IT Gene

expression, **.alpha.7.beta.1**

integrin; expression of the **alpha.7**

beta.1 integrin in skeletal muscle

development and **muscular dystrophy**

IT Development, mammalian postnatal

myogenesis; expression of the **alpha.7 beta.**

1 integrin in skeletal muscle development and
muscular dystrophy

II Integrins

RL: BPR Biological process ; BSU Biological study, unclassified ; BIL Biological study ; PROC Process
 .alpha.7.beta.1; expression of
 the alpha 7.beta.1
 integrin in skeletal muscle development and muscular
 dystrophy

136 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:808972 HCAPLUS

DN 108:100696

TI Altered expression of the .alpha.7.beta.
 1 integrin in human and murine muscular
 dystrophies

AU Hodges, B. L.; Hayashi, Y. K.; Nonaka, I.; Wang, W.; Aranata, K.;
 Kaufman, S. J.

CS Department of Cell and Structural Biology, University of Illinois, Urbana,
 IL, USA

SO Journal of Cell Science (1997), 110(22), 2873-2881

CIDEN: JNCSTAI; ISSN: 1021-9533

PB Company of Biologists Ltd.

DT Journal

LA English

CC 14-11 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 3

AB The .alpha.7.beta.1

integrin is the primary laminin receptor on skeletal myoblasts and
 adult myofibers. It has distinct functions during muscle development and
 contributes to muscle structural integrity. The authors have studied this
 integrin in cases where expression of dystrophin or
 laminin are compromised. Immunofluorescence demonstrates an increase in .
 alpha.7.beta.1 in patients with
 Duchenne muscular dystrophy and in mdx mice that lack
 dystrophin. Anal. of RNA from mdx mice and from patients with
 Duchenne and Becker muscular dystrophies indicates
 that the increase in the .alpha.7.beta.

1 integrin is regulated at the level of .alpha
 .7 gene transcription. In contrast, the levels of .
 alpha.7.beta.1 integrin

are severely diminished in patients with laminin .alpha.2 chain congenital
 dystrophy muscular dystrophy and in dy/dy mice
 that also do not make the .alpha.2 laminin chain. Anal. of RNA from the
 hindlimbs of dy/dy mice demonstrated that in the absence of laminin .
 alpha.7 gene transcription is inhibited and limited to
 specific alternatively spliced isoforms. The authors suggest that the
 increased expression of .alpha.7.beta.

1 integrin in the absence of dystrophin
 compensates for the reduced dystrophin-mediated linkage of
 fibers with the basal lamina and modulates the development of pathol.
 assocd. with these diseases. The decrease in .alpha.7

.beta.1 integrin and its transcripts in the
 absence of laminin likely contributes to the severe myopathy that results
 from laminin .alpha.2 chain deficiency and suggests that laminin-2
 regulates expression of the .alpha.7 integrin
 gene. The role of the .alpha.7.beta.

1 integrin in muscle integrity also suggests that
 compromised expression of this receptor may underlie as yet undefined
 myopathies.

BT alpha7beta1 integrin altered expression
 muscular dystrophy; gene expression alpha7beta1
 integrin muscular dystrophy

IT Laminins

EL: ADV Adverse effect, including toxicity ; BIO Biological occurrence ;

- BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Occurrence)
 (altered expression of .alpha.7.beta.
 1 integrin in human and murine muscular dystrophies in relation to)
- IT Muscular dystrophy
 Becker's; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies
- IT Muscular dystrophy
 (Duchenne; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)
- IT mRNA
 RL: AIV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFY (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)
 (altered expression of .alpha.7.beta.
 1 integrin in human and murine muscular dystrophies)
- IT Gene, animal
 RL: AIV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (altered expression of .alpha.7.beta.
 1 integrin in human and murine muscular dystrophies)
- IT Dystrophin
 RL: AIV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (altered expression of .alpha.7.beta.
 1 integrin in human and murine muscular dystrophies in relation to)
- IT Basement membrane
 (basal lamina; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies in relation to)
- IT Muscular dystrophy
 (congenital, merosin-deficient; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)
- IT Mouse
 (dy/dy and mdx; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)
- IT Gene
 (expression; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)
- IT CD antigens
 CD antigens
 Integrins
 Integrins
 RL: AIV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 integrin .alpha.7; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies
- IT RNA splicing
 messenger; altered expression of .alpha.7

- .beta.1 integrin in human and murine muscular dystrophies in relation to
- IT Transcription, genetic regulation; altered expression of .alpha.7 .beta.1 integrin in human and murine muscular dystrophies)
- IT Pre-mRNA
- RL: BPP (Biological process); BSU (Biological study, unclassified); BIOC (Biological study); PROC (Process) (splicing; altered expression of .alpha.7 .beta.1 integrin in human and murine muscular dystrophies in relation to)
- IT Integrins
- RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOC (Biological study); OCCU (Occurrence); PROC (Process) (.alpha.7.beta.1; altered expression of .alpha.7.beta.1 integrin in human and murine muscular dystrophies)

L36 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:000713 HCAPLUS

DN 118:12332

TI Absence of integrin .alpha.7 causes a novel form of muscular dystrophy

AU Mayer, Ulrike; Saher, Gesine; Fassler, Feinhard; Bornemann, Antje; Echtermeyer, Frank; von der Mark, Helga; Miosge, Nicolai; Poschl, Ernst; von der Mark, Klaus

CS Max-Planck-Inst. Biochem., Martinisried, D-82152, Germany

SO Nature Genetics (1997), 17(3), 318-323

CODEN: NGENEC; ISSN: 1061-4036

FB Nature America

ET Journal

LA English

CC 14-11 (Mammalian Pathological Biochemistry)

Section cross-references): 3

AB Integrin .alpha.7.beta.1

is a specific cellular receptor for the basement membrane protein laminin-1, as well as for the laminin isoforms -2 and -4. The .alpha.7 subunit is expressed mainly in skeletal and cardiac muscle and has been suggested to be involved in differentiation and migration processes during myogenesis. Three cytoplasmic and two extracellular splice variants that have been described are developmentally regulated and expressed in different sites in the muscle. In adult muscle, the .alpha.7A and .alpha.7B subunits are concd. in myotendinous junctions and along the sarcolemmal membrane. To study the potential involvement of .alpha.7 integrin during myogenesis a null allele of the .alpha.7 gene (itga7) in the germline of mice by homologous recombination in embryonic stem (ES) cells. Surprisingly, mice homozygous for the mutation are viable and fertile, indicating that the .alpha.7.beta.1 integrin is not essential for myogenesis. However, histol. anal. of skeletal muscle revealed typical symptoms of a progressive muscular dystrophy starting soon after birth, but with a distinct variability in different muscle types. The obsd. histopathol. changes strongly indicate an impairment of function of the myotendinous junctions. These findings demonstrate that .alpha.7.beta.1 integrin represents an indispensable linkage between the muscle fiber and the extracellular matrix that is independent of the dystrophin-dystroglycan complex-mediated interaction of the cytoskeleton with the muscle basement membrane.

- IT integrin alpha7 deficiency muscular dystrophy
- IT Alleles
 - Basement membrane
 - Extracellular matrix
 - Fertility
 - Heart
 - Muscle
 - (absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Disease, animal
 - (deficiency, integrin .alpha.7; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT CD antigens
 - CD antigens
 - Integrins
 - Integrins
- RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 - (integrin .alpha.7; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Gene, animal
 - RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 - (itga7; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Muscle
 - Muscle
 - Tendon
 - Tendon
 - (muscle-tendon junction; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Mutation
 - (null; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Muscular dystrophy
 - (progressive; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Cell membrane
 - (sarcolemma; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile)
- IT Integrins
 - RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 - .alpha.7.beta.1; absence of integrin .alpha.7 causes novel form of progressive muscular dystrophy although muscle development is normal and mice are fertile

- 100 ANSWER 10 OF 10 HEADLINE COPYRIGHT 1995 ADP
 101 1997:0502:000000000000
 102 127:8298800
 103
 104 **Integrins .alpha.7.beta.1**
 105 in muscle function and survival: disrupted expression in
 106 merosin-deficient congenital **muscular dystrophy**
 107 Vachon, Pierre H.; Xu, Hong; Liu, Ling; Loechel, Frosty; Hayashi, Yukiko;
 108 Arahata, Kiichi; Reed, John C.; Wewer, Ulla M.; Engvall, Eva
 109 La Jolla Cancer Research Center, The Burnham Institute, La Jolla, CA,
 110 92037, USA
 111 Journal of Clinical Investigation (1997), 100(7), 1671-1681
 112 CODEN: JCIHAC; ISSN: 0021-9738
 113 Rockefeller University Press
 114 Journal
 115 English
 116 14-11 (Mammalian Pathological Biochemistry)
 117 Section cross-reference(s): 13
 118 **AB** Mutations in genes coding for **dystrophin**, for .alpha., .beta.,
 119 .gamma., and .delta.-sarcoglycans, or for the .alpha.2 chain of the
 120 basement membrane component merosin (laminin-2/4) cause various forms of
 121 **muscular dystrophy**. Analyses of **integrins**
 122 showed an abnormal expression and localization of .alpha.
 123 **.beta.1** isoforms in myofibers of
 124 merosin-deficient human patients and mice, but not in **dystrophin**
 125 -deficient or sarcoglycan-deficient humans and animals. It was shown
 126 previously that skeletal muscle fibers require merosin for survival and
 127 function. Correction of merosin deficiency in vitro through cell
 128 transfection with the merosin .alpha.2 chain restored the normal
 129 localization of **.alpha.7.beta.1D integrins**
 130 as well as myotube survival. Overexpression of the apoptosis-suppressing
 131 mol. Bcl-2 also promoted the survival of merosin-deficient myotubes, but
 132 did not restore a normal expression of **.alpha.7**
 133 **.beta.1D integrins**. Blocking of **.beta.1**
 134 **integrins** in normal myotubes induced apoptosis and severely
 135 reduced their survival. These findings (a) identify **.alpha.**
 136 **.beta.1D integrins** as the de facto receptors for
 137 merosin in skeletal muscle; (b) indicate a merosin dependence for the
 138 accurate expression and membrane localization of **.alpha.**
 139 **.beta.1D integrins** in myofibers; (c) provide a mol.
 140 basis for the crit. role of merosin in myofiber survival; and (d) add new
 141 insights to the pathogenesis of neuromuscular disorders.
 142 **ST** **integrin alpha7beta1 merosin deficiency**
 143 **muscular dystrophy; muscle survival integrin**
 144 **alpha7beta1 merosin deficiency**
 145 Laminins
 146 **RT** ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
 147 BPR (Biological process); BSU (Biological study, unclassified); BICL
 148 (Biological study); OCCU (Occurrence); PROC (Process)
 149 (2, deficiency; **integrins .alpha.7**
 150 **.beta.1** in muscle function and survival and
 151 disrupted expression in merosin-deficient congenital **muscular**
 152 **dystrophy** in humans and mice
 153 **RT** Proteins, specific or class
 154 **RT** BPR (Biological process); BSU (Biological study, unclassified); BICL
 155 (Biological study); PROC (Process)
 156 Bcl-2, apoptosis suppression by; **integrins .alpha.**
 157 **.beta.1** in muscle function and survival
 158 and disrupted expression in merosin-deficient congenital
 159 **muscular dystrophy** in humans and mice in relation to
 160 **RT** **Muscular dystrophy**
 161 congenital, merosin-deficient; **integrins**
 162 **.alpha.7.beta.1** in muscle
 163 function and survival and disrupted expression in merosin-deficient

- congenital muscular dystrophy in humans and mice
- IT Disease, animal
 deficiency, merosin; **integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice
- IT Muscle
 (fiber; **integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT CD antigens
 CD antigens
Integrins
Integrins
 RL: ADV (Adverse effect, including toxicity); BCC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (integrin .alpha.7, A and B isoforms;
integrins (.alpha.7.beta.1) in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT Mutation
 (**integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT Gene, animal
 RL: ADV (Adverse effect, including toxicity); BCC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (**integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT Apoptosis
 (**integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice in relation to)
- IT Receptors
 RL: BCC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (merosin, integrin .alpha.7.beta.1D as;
integrins (.alpha.7.beta.1) in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT Integrins
 RL: ADV (Adverse effect, including toxicity); BCC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (.alpha.7.beta.1; **integrins (.alpha.7.beta.1)** in muscle function and survival and disrupted expression in merosin-deficient congenital muscular dystrophy in humans and mice)
- IT Integrins
 RL: ADV (Adverse effect, including toxicity); BCC (Biological occurrence); EPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

.beta.1, 1 isoform; integrins
.alpha.7.beta.1 in muscle
function and survival and disrupted expression in merosin-deficient
congenital muscular dystrophy in humans and mice

=> fill hepplus biosis

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- L52 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:352792 BIOSIS
DN PREV200100:52792
TI **Integrin alpha7beta1 in muscular dystrophy/myopathy of unknown etiology.**
AU Pegoraro, Elena (1); Depolliaro, Fulvio; Prandini, Paola; Marin, Alessandra; Fanin, Marina; Trevisan, Carlo P.; El-Messlemani, Abdul Hassik; Tarone, Guido; Engvall, Eva; Hoffman, Eric P.; Angelini, Corrado
CS 1) Neurocruscular Center, Department of Neurological and Psychiatric Sciences, University of Padova, 35128, Padova: elena.pegoraro@unipd.it Italy
SO American Journal of Pathology, (June, 2002) Vol. 160, No. 6, pp. 2135-2143. <http://ajp.amjpathol.org/>. print. ISSN: 0002-9440.
DT Article
LA English
AB To investigate the role of **integrin alpha7** in muscle pathology, we used a "candidate gene" approach in a large cohort of **muscular dystrophy/myopathy** patients. Antibodies against the intracellular domain of the **integrin alpha7A** and **alpha7B** were used to stain muscle biopsies from 210 patients with **muscular dystrophy/myopathy** of unknown etiology. Levels of **alpha7A** and **alpha7B integrin** were found to be decreased in 35 of 210 patients (approx17%). In six of these patients no **integrin alpha7B** was detected. Screening for **alpha7B** mutation in 30 of 35 patients detected only one **integrin alpha7** missense mutation (the mutation on the second allele was not found) in a patient presenting with a congenital **muscular dystrophy**-like phenotype. No **integrin alpha7** gene mutations were identified in all of the other patients showing **integrin alpha7** deficiency. In the process of mutation analysis, we identified a novel **integrin alpha7** isoform presenting 72-bp deletion. This isoform results from a partial deletion of exon 21 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position 2644 in **integrin alpha7** cDNA. This spliced isoform is present in about 11% of the chromosomes studied. We conclude that secondary **integrin alpha7** deficiency is rather common in **muscular dystrophy/myopathy** of unknown etiology, emphasizing the multiple mechanisms that may modulate **integrin** function and stability.
- CC Cytology and Cytochemistry - General *12511
Cytology and Cytochemistry - Human *12512
Genetics and Cytogenetics - General *12513
Genetics and Cytogenetics - Human *12514
Pathology, General and Miscellaneous - General *12515
Metabolism - Metabolic Disorders *12516

Muscle - Pathology; *H3574
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology; *H3575
 Nervous System - Pathology; *H3576
 EI Hominidae; *H3577
 IT Major Concepts
 Cell Biology; Molecular Genetics; Biochemistry and Molecular
 Biophysics; Neurology; Human Medicine, Medical Sciences; Orthopedics
 (Human Medicine, Medical Sciences); Pathology
 IT Diseases
 muscular dystrophy; myopathy of unknown etiology;
 etiology, genetics, muscle disease, nervous system disease, pathology;
 secondary **integrin alpha-7** deficiency;
 complications, metabolic disease, pathology
 IT Chemicals & Biochemicals
 integrin alpha-7-beta-1
 : function, stability
 IT Methods & Equipment
 mutation analysis: genetic method
 IT Miscellaneous Descriptors
 phenotype
 ORGN Super Taxa
 Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
 GEN human **integrin alpha-7** gene (Hominidae)

152 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2002:507438 BIOSIS

IN PREV200200507438

II Expression of **alpha7beta1 integrin** splicing variants
 during skeletal muscle regeneration.

AU Kaariainen, Minna; Nissinen, Liisa; Kaufman, Stephen;

Sonnenberg, Arnoud; Jarvinen, Markku; Heino, Jyrki; Kalimo, Hannu (1)

CS (1) Department of Pathology, Turku University Hospital, FIN-20520, Turku:
 rkalimo@utu.fi Finland

SO American Journal of Pathology, (September, 2002) Vol. 161, No. 3, pp.
 1023-1031. <http://ajp.amjpathol.org/>. print.
 ISSN: 0002-9440.

BT Article

LA English.

AB **Integrin alpha7beta1** is a laminin receptor, both subunits of which have alternatively spliced, developmentally regulated variants. In skeletal muscle **beta1** has two major splice variants of the intracellular domain (**beta1A** and **beta1I**). **alpha7X1** and **alpha7X2** represent variants of the **alpha7** ectodomain, whereas **alpha7A** and **alpha7B** are variants of the intracellular domain. Previously we showed that during early regeneration after transection injury of muscle **alpha7 integrin** mediates dynamic adhesion of myofibers along their lateral aspects to the extracellular matrix. Stable attachment of myofibers to the extracellular matrix occurs during the third week after injury, when new myotendinous junctions develop at the ends of the regenerating myofibers. Now we have analyzed the relative expression of **beta1A**, **beta1I** and **alpha7A**, **alpha7B** and **alpha7X1**, **alpha7X2** isoforms during regeneration for 1 to 16 days after transection of rat's longissimus muscle using reverse transcriptase-polymerase chain reaction and immunoblot chemistry. During early regeneration **beta1A** was the predominant isoform in both the muscle and scar tissue. Expression of muscle-specific **beta1I** was detected in regenerating myofibers from day 4 onwards, i.e., when myoblastic mitotic activity began to decrease, and it became more abundant with the progression of regeneration. **alpha7B** isoform predominated on day

1. Thereafter, the relative expression of **alpha7A** transcripts increased until day 7 with the concomitant appearance of **alpha7A** immunoreactivity in regenerating myofibers. Finally, **alpha7B** again became the predominant variant in highly regenerated myofibers. Similarly as in the controls, **alpha7X1** and **alpha7X2** isoforms were both expressed throughout the regeneration with a peak in **alpha7X1** expression on day 4 coinciding with the dynamic adhesion stage. The results suggest that during regeneration of skeletal muscle the splicing of **beta1** and **alpha7 integrin** subunits is regulated according to functional requirements. **alpha7A** and **alpha7X1** appear to have a specific role during the dynamic phase of adhesion, whereas **alpha7B**, **alpha7X2**, and **beta1D** predominate during stable adhesion.

CC Biochemical Studies - General *10060
 BC Muscle - Physiology and Biochemistry *17504
 BC Muridae 36375
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Muscular System (Movement and Support)
 IT Parts, Structures, & Systems of Organisms
 skeletal muscle: muscular system, regeneration
 IT Chemicals & Biochemicals
 alpha-7-beta-1 integrin
 splicing variants: expression
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 Sprague-Dawley rat (Muridae): adult, male
 ORGN Organism Superterms
 Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L52 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2002:369184 BIOSIS
 DN PREV200200369184
 TI **Integrin**-mediated complementary gene therapy in muscle disease.
 AU Burkin, Dean J. (1); Wallace, Gregory Q. (1); Milner, Derek (1); Chaney, Eric (1); Kaufman, Stephen J. (1)
 CS (1) Cell and Structural Biology, University of Illinois, 601 S. Goodwin Ave, Urbana, IL, 61801 USA
 SO FASEB Journal, March 20, 2002 Vol. 16, No. 4, pp. A726.
 http://www.fasebj.org/. print.
 Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
 ISSN: 0892-6638.
 DT Conference
 LA English
 AB The molecular continuity between the extracellular matrix and cell cytoskeleton is essential for the structural and functional integrity of skeletal and cardiac muscle. Muscle fibers attach to laminin in the basal lamina using two distinct linkage systems, the dystrophin glycoprotein complex and the **alpha7beta1 integrin**. Mutations in the dystrophin gene that result in an absence of the dystrophin protein cause Duchenne Muscular Dystrophy (DMD) and affect 1 in 3,500 newborn males. To test whether elevated levels of the **alpha7 integrin** can compensate for the absence of dystrophin, we expressed the rat **alpha7** chain in mdx utr -/- mice that lack both dystrophin and utrophin. These mice develop a severe muscular dystrophy highly akin to DMD and die prematurely. The transgenic expression of the **alpha7BX2** chain in the mdx utr -/- mice reduced the development of skeletal and cardiac muscle disease and increased the longevity of the mice three-fold. This suggests that complementary gene therapy, based on the enhanced expression of the

alpha7beta1 integrin, may provide a novel approach to treat DMD.

- CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *11821
- Genetics and Cytogenetics - Human *13504
- Biochemical Studies - Proteins, Peptides and Amino Acids *11164
- Muscle - Physiology and Biochemistry *17504
- Muscle - Pathology *17506
- Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18016
- BC Hominidae 86215
- Muridae 86375
- IT Major Concepts
 - Medical Genetics (Allied Medical Sciences); Orthopedics (Human Medicine, Medical Sciences)
- IT Parts, Structures, & Systems of Organisms
 - skeletal muscle: differentiation, muscular system
- IT Diseases
 - Duchenne muscle dystrophy: muscle disease, therapy
- IT Chemicals & Biochemicals
 - alpha-7-beta-1 integrin**
 - ; dystrophin; utrophin
- IT Methods & Equipment
 - integrin-mediated complementary gene therapy: gene therapy**
 - method
- IT Miscellaneous Descriptors
 - Meeting Abstract
- ORGN Super Taxa
 - Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 - human (Hominidae); mouse (Muridae)
- ORGN Organism Superterms
 - Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates
- GEN human dystrophin gene (Hominidae): mutations
- L52 ANSWER 16 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- AN 2003:166691 BIOSIS
- DN PFEV2003(0166691
- TI **Integrin** is a compensatory transmembrane linkage to sarcoglycan in muscle.
- AU Allikian, M. J. (1); Hack, A. A. (1); Mewborn, S. (1); Meyer, U.; McNally, E. M. (1)
- CS 1. Medicine, University of Chicago, Chicago, IL, USA USA
- SO Molecular Biology of the Cell, (Nov. 2002, 2002) Vol. 13, No. Supplement, pp. 318a. print.
- Meeting Info.: 42nd Annual Meeting of the American Society for Cell Biology San Francisco, CA, USA December 14-18, 2002 American Society for Cell Biology
- . ISSN: 1059-1524.
- BT Conference
- LA English
- CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *11821
- Biochemical Studies - General *11164
- Biochemical Studies - Proteins, Peptides and Amino Acids *11164
- Cardiovascular System - Heart Pathology *14504
- Muscle - Physiology and Biochemistry *17504
- Muscle - Pathology *17506
- Nervous System - Pathology *21504
- BC Muridae 86375
- IT Major Concepts
 - Biochemistry and Molecular Biophysics; Muscular System Movement and

- Support
- IT Parts, Structures, & Systems of Organisms
 - muscle: muscular system; plasma membrane
- IT Diseases
 - cardiomyopathy: heart disease; **muscular dystrophy:** muscle disease, nervous system disease
- IT Chemicals & Biochemicals
 - dystroglycan; dystrophin; gamma-sarcoglycan; **integrin:** compensatory transmembrane linkage; **integrin-alpha-7-beta-1;** myosin heavy chain; sarcoglycan
- IT Alternate Indexing
 - Cardiomyopathy, Congestive (MeSH); **Muscular Dystrophies (MeSH)**
- IT Methods & Equipment
 - histologic examination: histology and cytology techniques, laboratory techniques; immunostaining: immunologic techniques, laboratory techniques
- IT Miscellaneous Descriptors
 - Meeting Abstract
- ORGN Super Taxa
 - Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 - mouse (Muridae)
- ORGN Organism Superterms
 - Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
- FN 153-17-00 **INTEGRIN**
00791-49-00 (**INTEGRIN**)
- 152 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- AN 2002:55330 BIOSIS
- EN PREV2002 55332
- TI **Integrin alpha7beta1 in muscular dystrophy** myopathy of unknown etiology.
- AU Pegoraro, Elena (1); Prandini, Paola (1); Fanin, Marina (1); Tarone, Guido; Enqvall, Eva; Angelini, Corrado (1)
- CS 1) Padova Italy
- SO Neurology, (April 9, 2002) Vol. 58, No. 7 Supplement 3, pp. A316.
<http://www.neurology.org/>. print.
Meeting Info.: 14th Annual Meeting of the American Academy of Neurology
Denver, Colorado, USA April 13-20, 2002
ISSN: 0028-3878.
- BT Conference
- LA English
- CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00523
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Human *03506
Pathology, General and Miscellaneous - Diagnostic *12504
Muscle - Physiology and Biochemistry *17504
Muscle - Pathology *17506
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18114
Nervous System - Pathology *21506
- BT Humanidae *6015
- IT Major Concepts
 - Medical Genetics (Allied Medical Sciences ; Anthropology Human Medicine, Medical Sciences)
- IT Parts, Structures, & Systems of Organisms
 - muscle: muscular system
- IT Diseases
 - muscular dystrophy:** etiology, genetics, muscle disease, nervous system disease; myopathy: etiology, genetics, muscle disease

IT Chemicals & Biochemicals
 integrin alpha-7: intracellular domain
 IT Alternate Indexing
 Muscular Dystrophy MeSH
 IT Methods & Equipment
 muscle biopsy: diagnostic method
 IT Miscellaneous Descriptors
 Meeting Abstract; Meeting Poster
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
 GEN human **integrin alpha-7** gene (Hominidae):
 missense mutations

L82 ANSWER 18 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2002:427550 BIOSIS

DN PREV200201427550

TI Localization of **alpha7 integrins** and dystrophin
 suggests potential for both lateral and longitudinal transmission of
 tension in large mammalian muscles.

AU Paul, Angelika D.; Sheard, Philip W.; Kaufman, Stephen J.;
 Duxson, Marilyn J. (1)

CS (1) Department of Anatomy and Structural Biology, University of Otago, PO
 Box 913, Dunedin, 9001: marilyn.duxson@stonebow.otago.ac.nz New Zealand

SO Cell & Tissue Research, (May, 2002) Vol. 308, No. 2, pp. 255-265. print.
 ISSN: 0302-760X.

DT Article

LA English

AB Non-primate mammalian muscles with fascicles above 35 mm in length are
 composed predominantly of arrays of short, non-spanning muscle fibres,
 which terminate within the belly of the muscle fascicle at one or both
 ends. We have previously described the morphological form of various
 muscle-to-muscle and muscle-to-matrix junctions which are likely involved
 in tension transmission within one such muscle - the guinea pig
 sternomastoid muscle (Young et al. 2000). Here, we use
 immunohistochemistry to investigate the cell adhesion molecules present at
 these junctions. We find strong immunoreactivity against the
alpha7B integrin subunit and dystrophin, and slight
 reactivity against the **alpha7A integrin** at all
 intrafascicular fibre terminations (IFTs), as well as at the muscle-tendon
 junction (MTJ). Tenascin, the sole ligand for **alpha9beta1 integrin**
 , was absent from IFTs but present at the MTJ, suggesting the two sites
 are molecularly distinct. In addition to their expression at junctional
 sites, **alpha7B integrin** and dystrophin were also
 expressed ubiquitously along the non-junctional sarcolemma, suggesting
 potential involvement in diffuse lateral transmission of tension between
 adjacent fibres. We conclude that the distribution of **alpha7beta1**
integrins and dystrophin in series-fibred muscles suggests they
 are involved in transmission of tension from intrafascicularly terminating
 fibres to neighbouring fibres lying both in-series and in-parallel, via
 the extracellular matrix (ECM).

WC Biochemical Studies - Proteins, Peptides and Amino Acids *1784

Muscle - Physiology and Biochemistry *1784

EC Caviidae *6331

Muridae *6375

IT Major Concepts

 Muscular System: Movement and Support

IT Parts, Structures, & Systems of Organisms

 anterior gracilis muscle: muscular system; sternomastoid muscle:
 muscular system

17 Chemicals & Biochemicals

alpha-7 integrins: large mammalian muscle

localization, lateral tension transmission role, longitudinal tension transmission role; dystrophin: large mammalian muscle localization, lateral tension transmission role, longitudinal tension transmission role

ORGN Super Taxa

Caviidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

guinea pig (Caviidae): animal model; rat (Muridae): animal model

ORGN Organism Superterms

Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L52 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2000:461479 BIFSIS

DN PFEV200000460479

TI Laminin and **alpha7betal integrin** regulate

agrin-induced clustering of acetylcholine receptors.

AU Burkin, Dean J.; Kim, Jae Eun; Gu, Maojian; Kaufman, Stephen J.

(1)

CS (1) Department of Cell and Structural Biology, University of Illinois, Urbana, IL, 61801 USA

SO Journal of Cell Science, (August, 2000) Vol. 113, No. 16, pp. 2877-2886.

print.

ISSN: 0021-9533.

DT Article

LA English

SL English

AB The clustering of acetylcholine receptors (AChRs) in the post-synaptic membrane of skeletal muscle is an early developmental event in the formation of the neuromuscular junction. Several studies show that laminin, as well as neural agrin, can induce AChR clustering in C2C12 myofibers. We recently showed that specific isoforms of the **alpha7betal integrin** (a receptor normally found at neuromuscular junctions) colocalize and physically interact with AChR clusters in a laminin-dependent fashion. In contrast, induction with agrin alone fails to promote localization of the **integrin** with AChR clusters. Together both agrin and laminin enhance the interaction of the **integrin** with AChRs and their aggregation into clusters. To further understand this mechanism we investigated cluster formation and the association of the **alpha7betal integrin** and AChR over time following induction with laminin and/or agrin. Our results show that the **alpha7betal integrin** associates with AChRs early during the formation of the post-synaptic membrane and that laminin modulates this recruitment. Laminin induces a rapid stable association of the **integrin** and AChRs and this association is independent of clustering. In addition to laminin-1, merosin (laminin-2/4) is present both before and after formation of neuromuscular junctions and also promotes AChR clustering and colocalization with the **integrin** as well as synergism with agrin. Using site directed mutagenesis we demonstrate that a tyrosine residue in the cytoplasmic domain of both **alpha7A** and **alpha7B** chains regulates the localization of the **integrin** with AChR clusters. We also provide evidence that laminin, through its association with the **alpha7betal integrin**, reduces by 21-fold the concentration of agrin required to promote AChR clustering and accelerates the formation of clusters. Thus laminin, agrin and the **alpha7betal integrin** act in a concerted manner early in the development of the post-synaptic membrane, with laminin priming newly formed myofibers to rapidly and vigorously respond to low concentrations of neural agrin produced by innervating motor neurons.

CC Cytology and Cytochemistry - Animal *10514
 Biochemical Studies - Proteins, Peptides and Amino Acids *10704
 Muscle - Physiology and Biochemistry *17504
 Nervous System - Physiology and Biochemistry *20504
 IT Major Concepts
 Muscular System (Movement and Support); Nervous System (Neural Coordination)
 IT Parts, Structures, & Systems of Organisms
 motor neurons: nervous system; myofiber: muscular system; neuromuscular junction: formation, nervous system; post-synaptic membrane: formation, nervous system
 IT Chemicals & Biochemicals
 acetylcholine receptors [AChRs]: cluster formation, localization; agrin; **alpha-7-A chain**: tyrosine residue; **alpha-7-B chain**; **alpha-7-beta-1 integrin**: localization, regulation; laminin-1; merosin [laminin-2/4]; tyrosine
 RN 100-13-40 (TYROSINE)
 500-13-60 (TYROSINE)

L52 ANSWER 20 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1000:20768 BIOSIS
 DN PREVL100000160768
 IT Interaction of the **alpha7beta1 integrin** and acetylcholine receptor during formation of the neuromuscular junction.
 AU Kaufman, Stephen J. (1); Burkin, Dean J. (1)
 CS 1 University of Illinois, 601 S. Goodwin Ave., B107 CLSL, Urbana, IL USA
 SC Molecular Biology of the Cell, (Nov., 1999) Vol. 10, No. SUPPL., pp. 353a.
 Meeting Info.: 39th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 11-15, 1999 The American Society for Cell Biology
 . ISSN: 1099-1524.
 DT Conference
 LA English
 CC Biochemical Studies - General *10060
 Cytology and Cytochemistry - General *02502
 Biophysics - Membrane Phenomena *10508
 Nervous System - Physiology and Biochemistry *20504
 Muscle - Physiology and Biochemistry *17504
 General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Nervous System (Neural Coordination)
 IT Chemicals & Biochemicals
 acetylcholine receptor; agrin; **alpha-7-beta-1 integrin**; laminin
 IT Miscellaneous Descriptors
 muscle fiber; neuromuscular junction: formation; Meeting Abstract

L52 ANSWER 21 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1999:188029 BIOSIS
 DN PREVL199900355029
 IT A functional role for specific isoforms of the **alpha7beta1 integrin** in the early development of acetylcholine receptor clusters.
 AU Burkin, D. J. (1); Gu, M. (1); Wallace, G. L. (1); Kaufman, S. J. (1)
 CS 1 University of Illinois, Urbana, IL USA
 SC Developmental Biology, (June 1, 1999) Vol. 111, No. 1, pp. 141.
 Meeting Info.: 59th Annual Meeting of the Society for Developmental Biology Charlottesville, Virginia, USA June 13-18, 1999 Society for Developmental Biology

. ISSN: 1011-1016.
IT Conference
LA English
SC Developmental Biology - Embryology - General and Descriptive *10111
Microscopy Techniques - General and Special Techniques *01011
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10111
Nervous System - General; Methods *20501
Muscle - General; Methods *17511
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Mammalia - Unspecified 85700
IT Major Concepts
Biochemistry and Molecular Biophysics; Development; Muscular System (Movement and Support)
IT Parts, Structures, & Systems of Organisms
muscle: muscular system; neuromuscular junction: nervous system
IT Chemicals & Biochemicals
acetylcholine receptor clusters; **alpha7beta1 integrin**
: functional role, isoforms
IT Methods & Equipment
immunofluorescence microscopy: microscopy method; immunoprecipitation: analytical method; Western analysis: analytical method
IT Miscellaneous Descriptors
embryogenesis; Meeting Abstract
ORGN Super Taxa
Mammalia: Vertebrata, Chordata, Animalia
ORGN Organism Name
mammal (Mammalia): embryo
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
FN 153-87-72 (INTEGRIN)
01791-44-12 (INTEGRIN)
51-84-3 (ACETYLCHOLINE)

L52 ANSWER 22 OF 29 EICISIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:199812 EICISIS

DN PREV199801156802

TI Mutations in the **integrin alpha7** gene cause congenital myopathy.

AU Hayashi, Yukiko K.; Chou, Fan-Li; Engvall, Eva; Ogawa, Megumu; Matsuda, Onie; Hirabayashi, Shinichi; Yokochi, Kenji; Zieber, Barry L.; Kramer, Randall H.; **Kaufman, Stephen J.**; Ozawa, Eihiro; Goto, Yu-ichi; Nonaka, Ikuya; Tsukahara, Toshifumi; Wang, Jian-Zhou; Hoffman, Eric P.; Arahata, Hiichi (1)

CS (1) Dep. Neuromuscular Res., Natl. Inst. Neurosci., Natl. Cent. Neurol. Psychiatry, Kodaira, Tokyo 167-8502 Japan

SO Nature Genetics, (May, 1998) Vol. 19, No. 1, pp. 94-97.
ISSN: 1061-4036.

BT Article

LA English

AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin alpha7beta1D**. **Integrin beta1** is expressed throughout the body, while **integrin alpha7** is more muscle-specific. To address the role of **integrin alpha7** in human muscle disease, we determined **alpha7** protein expression in muscle biopsies from 11 patients with unclassified congenital myopathy and congenital muscular dystrophy by immunocytochemistry. We found three unrelated patients with **integrin alpha7** deficiency and normal laminin alpha2 chain expression. To determine if any of these three

patients had mutations of the **integrin alpha7** gene, ITGA7, we cloned and sequenced the full-length human ITGA7 cDNA, and screened the patients for mutations. The patient had splice mutations on both alleles; one causing a 31-bp insertion in the conserved cysteine-rich region, and the other causing a 98-bp deletion. A second patient was a compound heterozygote for the same 98-bp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of ITGA7 mRNA. Clinically, these patients showed congenital myopathy with delayed motor milestones. Our results demonstrate that mutations in ITGA7 are involved in a form of congenital myopathy.

CC Genetics and Cytogenetics - Human *03808
Biophysics - General Biophysical Techniques *10504
Enzymes - Methods *10804
Muscle - Pathology *17506
Nervous System - Pathology *20506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
BC Hominidae *6215
IT Major Concepts
Genetics; Muscular System (Movement and Support)
IT Diseases
congenital **muscular dystrophy**: congenital disease,
nervous system disease, genetic disease; congenital myopathy:
congenital disease, muscle disease
IT Chemicals & Biochemicals
cDNA [complementary DNA]; **integrin alpha-7**
gene: mutation; **integrin alpha-7** protein:
expression; mRNA [messenger RNA]
IT Methods & Equipment
immunoblotting: analytical method, detection/labeling techniques;
immunocytochemistry: analytical method, detection/labeling techniques;
RT-PCR [reverse transcriptase-polymerase chain reaction]: amplification
method, quantitation method, amplification techniques; SDS-PAGE
[SDS-polyacrylamide gel electrophoresis]: electrophoretic techniques,
separation method
IT Miscellaneous Descriptors
research
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

152 ANSWER 23 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1997:486215 BIOSIS

DI PREV199799755428

TI The **alpha-7-beta-1**

integrin mediates adhesion and migration of skeletal myoblasts on laminin.

AF Crawley, Suzanne; Farrell, Eleanor M.; Wang, Weigwang; Gu, Mactian; Huang, Hui-Yu; Huynh, Vu; Hodges, Bradley L.; Cooper, Douglas M. W. 11 ;
Kaufman, Stephen J.

1 LPP1-Box F-1084, 411 Parnassus Ave., San Francisco, CA 94143 USA

Experimental Cell Research, 1997, Vol. 231, No. 1, pp. 274-280.
ISSN: 0014-4827.

IT Article

LA English

AB Many aspects of myogenesis are believed to be regulated by myoblast interactions with specific components of the extracellular matrix. For example, laminin has been found to promote adhesion, migration, and proliferation of mammalian myoblasts. Based on affinity chromatography, the **alpha-7-beta-1**

integrin has been presumed to be the major receptor mediating myoblast interactions with laminin. We have prepared a monoclonal antibody, Q26, that specifically reacts with both the $\alpha 1$ and the $\alpha 2$ extracellular splice variants of the **alpha-7 integrin** chain. This antibody completely and selectively blocks adhesion and migration of rat L8E63 myoblasts on laminin-1, but not on fibronectin. In contrast, a polyclonal antibody to the fibronectin receptor, **alpha-5-beta-1 integrin**, blocks myoblast adhesion on fibronectin, but not on laminin-1. The **alpha-7-beta-1 integrin** also binds to a mixture of laminin-2 and laminin-4, the major laminin isoforms in developing and adult skeletal muscle, but Q26 is a much less potent inhibitor of myoblast adhesion on the laminin-2/4 mixture than on laminin-1. Based on affinity chromatography, we suggest that this may be due to higher affinity binding of alpha-7X1 to laminin-2/4 than to laminin-1.

- CC Cytology and Cytochemistry - Animal *02506
- Biochemical Studies - Proteins, Peptides and Amino Acids *10064
- Biochemical Studies - Carbohydrates *10068
- Biophysics - Molecular Properties and Macromolecules *10506
- Biophysics - Membrane Phenomena *10508
- Muscle - Physiology and Biochemistry *17504
- In Vitro Studies, Cellular and Subcellular *32600
- BC Muridae *86378
- IT Major Concepts
 - Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology); Muscular System (Movement and Support)
- IT Chemicals & Biochemicals
 - INTEGRIN**
- IT Miscellaneous Descriptors
 - ADHESION; **ALPHA-7-BETA-1**
 - INTEGRIN**; BIOCHEMISTRY AND BIOPHYSICS; CELL BIOLOGY;
 - FIBRONECTIN; LAMININ; L8E63 CELL LINE; MIGRATION; MOUSE MYOBLAST;
 - MUSCULAR SYSTEM; RAT MYOBLASTS; SKELETAL MUSCLE DEVELOPMENT; SKELETAL MYOBLAST
- ORGN Super Taxa
 - Muridae; Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 - Q2C12 (Muridae): cell line
- ORGN Organism Superterms
 - animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 - rodents; vertebrates
- RN 153-37-70 (**INTEGRIN**)
- 60791-44-32 (**INTEGRIN**)
- 152 ANSWER 14 IF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- AN 1997:94024 BIOSIS
- DN PREV199799393897
- TI Comparison of rat myoblast receptors for laminin-1 and laminin-2/4.
- AF Crawley, S. C. (1); Kaufman, S. J.; Clasper, D. N. W.
- CC (1), Dep. Psychiatry, University California, San Francisco, CA 94143 USA
- CC Molecular Biology of the Cell, 1996, Vol. 7, No. SUPPL., pp. 67A.
- CC Meeting Info.: Annual Meeting of the 6th International Congress on Cell Biology and the 6th American Society for Cell Biology San Francisco, California, USA December 7-11, 1996
- ISSN: 1042-1524.
- IT Conference; Abstract; Conference
- LA English
- CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *15121
- Cytology and Cytochemistry - Animal *12506
- Biochemical Studies - General *10061
- Biophysics - General Biophysical Studies *10501

EC Muridae *14075
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology
 IT Chemicals & Biochemicals
 INTEGRIN
 IT Miscellaneous Descriptors
 ALPHA-7-BETA-1 INTEGRIN
 ; LAMININ 1; LAMININ 1 RECEPTOR; LAMININ-2/4; LAMININ-2/4 RECEPTOR;
 MEMBRANES; MYOBLAST
 ORGN Super Taxa
 Muridae; Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rat (Muridae)
 ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates
 RN 113-87-7Q (**INTEGRIN**)
 11791-49-3Q (**INTEGRIN**)
 L52 ANSWER 25 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1994:327133 BIOSIS
 DN FHEV199407340231
 TI Developmental regulation of the structure and function of **alpha-7-beta-1 integrin** in skeletal muscle.
 AU Wang, Weigwang; Kaufman, Stephen J.
 CS Dep. Cell and Structural Biol., Univ. Ill., Urbana, IL 61801 USA
 SO Journal of Cellular Biochemistry Supplement, (1994) Vol. 8, No. 18D, pp. 512.
 Meeting Info.: Keystone Symposium on Molecular Biology of Muscle Development Snowbird, Utah, USA April 11-17, 1994
 ISSN: 0733-1959.
 DT Conference
 LA English
 CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
 Cytology and Cytochemistry - Animal *02506
 Genetics and Cytogenetics - Animal *03506
 Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052
 Biochemical Methods - Proteins, Peptides and Amino Acids 10054
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Replication, Transcription, Translation *10300
 Biophysics - Molecular Properties and Macromolecules 10506
 Biophysics - Membrane Phenomena *10508
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Muscle - Physiology and Biochemistry *17504
 Developmental Biology - Embryology - Morphogenesis, General *25505
 EC Vertebrata - Unspecified *85150
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology; Development;
 Genetics; Membranes; Cell Biology; Metabolism; Molecular Genetics
 Biochemistry and Molecular Biophysics; Muscular System; Movement and Support.
 IT Chemicals & Biochemicals
 INTEGRIN; ACTIN
 IT Miscellaneous Descriptors
 ACTIN; FIBRONECTIN; GENE EXPRESSION; LAMININ; MEETING ABSTRACT; MEETING POSTER; RNA
 ORGN Super Taxa
 Vertebrata - Unspecified: Vertebrata, Chordata, Animalia
 ORGN Organism Name

Vertebrata Vertebrata - Unspecified
 ORGN Organism Superterms
 animals; chordates; nonhuman vertebrates; vertebrates
 RN 153-87-71 INTEGRIN
 60791-49-3Q INTEGRIN
 132579-21-8 (ACTIN)

LSZ ANSWER 26 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1994:325158 BIOSIS
 DN PREV199497336158
 TI Developmental regulation of the interaction of alpha-7
 -beta-1 integrin and extracellular matrix in
 skeletal muscle.
 AU Kaufman, Stephen J.; Song, Woo Keun; Sato, Hiro; Wang, Weigwang
 CS Dep. Cell and Structural Biol., Univ. Ill., Urbana, IL 61801 USA
 SO Journal of Cellular Biochemistry Supplement, (1994) Vol. 2, No. 160, pp.
 250.
 Meeting Info.: Keystone Symposium on Biology of Physicochemical
 Interactions at the Cell Surface Taos, New Mexico, USA February 20-26,
 1994
 ISSN: 0733-1959.
 DT Conference
 LA English
 CC General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annuals 00520
 Cytology and Cytochemistry - Human *02508
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Enzymes - Physiological Studies *10808
 Muscle - Physiology and Biochemistry *17504
 BC Hominidae *86215
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology; Enzymology
 (Biochemistry and Molecular Biophysics); Muscular System (Movement and
 Support)
 IT Chemicals & Biochemicals
 INTEGRIN
 IT Sequence Data
 amino acid sequence
 IT Miscellaneous Descriptors
 FIBRONECTIN; LAMININ; MEETING ABSTRACT; MEETING POSTER; MYOBLASTS; RNA;
 TYROSINE PHOSPHATASE
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae)
 ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates
 RN 153-87-7Q INTEGRIN
 60791-49-3Q INTEGRIN

LSZ ANSWER 27 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1994:162130 BIOSIS
 DN PREV199497175130
 TI Selective modulation of the interaction of alpha-7-
 beta-1 integrin with fibronectin and laminin
 by L-14 lectin during skeletal muscle differentiation.
 AU Gu, Macqian; Wang, Weigwang; Song, Woo Keun; Cooper, Douglas N. W.;
 Kaufman, Stephen J. (1)
 CS Dep. Cell Structural Biol., Univ. Illinois, Urbana, IL 61801 USA
 SO Journal of Cell Science, 1994 Vol. 107, No. 1, pp. 187-191.
 ISSN: 0021-9636.
 IT Article

- LA English
- AB The **alpha-7-beta-1 integrin** was originally identified and isolated from differentiating skeletal muscle and shown to be a laminin-binding protein (Song et al. (1992) J. Cell Biol. 117, 648-657). Expression of the **alpha-7** gene and protein are developmentally regulated during skeletal muscle differentiation and have been used to identify cells at distinct stages of the myogenic lineage (George-Weinstein et al. (1993) Dev. Biol. 156, 209-229). The lactoside-binding protein L-14 exists as a dimer and has been localized on a variety of cells, in association with extracellular matrix. During myogenesis in vitro, L-14 is synthesized within replicating myoblasts but it is not secreted until these cells commence terminal differentiation and fusion into multinucleate fibers (Cooper and Barondes, J. Cell Biol. (1990) 110, 1691-1691). Addition of purified L-14 to myogenic cells plated on laminin inhibits myoblast spreading and fusion, suggesting that the L-14 lectin regulates muscle cell interactions with the extracellular matrix that are germane to myogenic development (Cooper et al. (1991) J. Cell Biol. 115, 1437-1448). We demonstrate here, using affinity chromatography and immunoblots, that **alpha-7-beta-1** also binds to fibronectin and to the L-14 lectin. L-14 binds to both laminin and to the **alpha-7-beta-1 integrin**, and it can effectively inhibit the association of laminin and this **integrin**. Modulation of **alpha-7-beta-1** interaction with its ligands by L-14 is selective: L-14 does not bind to fibronectin, nor does it interfere with the binding of fibronectin to **alpha-7-beta-1**. These results are discussed in the context of the potential roles of **alpha-7-beta-1** in its interaction with laminin and fibronectin during myogenesis.
- CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Muscle - Physiology and Biochemistry *17534
Developmental Biology - Embryology - Morphogenesis, General *25508
- BC Muridae *86375
- IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Development; Muscular System (Movement and Support)
- IT Chemicals & Biochemicals
INTEGRIN
- IT Miscellaneous Descriptors
EXTRACELLULAR MATRIX; LACTOSIDE BINDING PROTEIN L-14; MYOBLAST; MYOGENESIS; MYOGENIC CELL
- ORGN Super Taxa
Muridae; Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
rat (Muridae)
- ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
- EN 183-87-70 **INTEGRIN**
60731-49-32 **INTEGRIN**
- DOI ANSWER 26 OF 29 BISSIC COPYRIGHT 1993 BIOLOGICAL ABSTRACTS INC.
AN 1994:21094 BIONIS
IN PREVIEW 1994:21094
IT **Alpha-7-beta-1 Integrin**
is a component of the myotendinous junction in skeletal muscle.
AU Bao, L. D. J.; Lakshminarayanan, M.; Kaufman, S.; Horwitz, A. F.
CF 1 Dep. Cell Structural Biol., Univ. Illinois Urbana-Champaign, Urbana, IL 61801 USA
JO Journal of Cell Science, 1993 Vol. 106, No. 2, pp. 573-583.
ISSN: 0021-9593.

- IT Article
 LA English
 AB Immunization against a 71 kDa band that co-purifies with skeletal muscle **integrins** has resulted in an antibody directed against the avian **alpha-7 integrin** subunit. The specificity of the antibody was established by patterns of tissue staining and cross-reactivity with antibodies directed against the cytoplasmic domain of the rat **alpha-7** cytoplasmic domain. On sections of adult skeletal muscle the **alpha-7 integrin** was enriched in the myotendinous junction (MTJ). This localization was unique as neither the **alpha-1**, **alpha-3**, **alpha-5**, **alpha-6** and **alpha-v** subunit localizes in the myotendinous junction. The distribution of the **alpha-7** subunit in the MTJ was examined during embryonic development. **alpha-7** expression in the junction is first apparent around embryo day 14 and is almost exclusively at the developing MTJ at this stage. **alpha-3** is expressed with distinctive punctate staining around the junctional area in earlier embryos (11-day). The time of appearance of the **alpha-7** subunit in the MTJ correlates with the insertion of myofibrils into subsarcolemmal densities and folding of the junctional membrane, suggesting a role of the **alpha-7 integrin** in this process. Vinculin is present throughout development of the myotendinous junction, suggesting that the **alpha-7 integrin** recognizes a preformed cytoskeletal structure. The presence of the **alpha-7** subunit in the myotendinous junction and the **alpha-5** subunit in the adhesion plaque demonstrates a molecular difference between these two adherens junctions. It also points to possible origins of junctional specificity on muscle. Differences between these two junctions were developed further using an antibody against phosphotyrosine (PY20). Phosphotyrosine is thought to participate in the organization and stabilization of adhesions. The focal adhesion and the neuromuscular junction, but not the MTJ, contained proteins phosphorylated on tyrosine.
- CC Cytology and Cytochemistry - Animal *02506
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Biophysics - Membrane Phenomena *10506
 Muscle - Physiology and Biochemistry *17504
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18014
 Developmental Biology - Embryology - General and Descriptive *25502
 Developmental Biology - Embryology - Morphogenesis, General *25508
- BC Muridae *80515
- IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology; Development; Membranes (Cell Biology); Muscular System (Movement and Support); Skeletal System (Movement and Support)
- IT Chemicals & Biochemicals
 INTEGRIN; PHOSPHOTYROSINE
- IT Miscellaneous Descriptors
 CYTOSKELETON; EMBRYONIC DEVELOPMENT; MUSCLE DEVELOPMENT; PHOSPHOTYROSINE
- EPCN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- EPCN Organism Name
 rat Muridae
- EPCN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
- BN 188-87-71 **INTEGRIN**
 60791-49-8 **INTEGRIN**
 21820-81-2 **PHOSPHOTYROSINE**

AN 1992:000000 BIOSIS
 CN BAP4:29174
 TI H36-**ALPHA-7** IS A NOVEL INTEGRIN ALPHA CHAIN
 THAT IS DEVELOPMENTALLY REGULATED DURING SKELETAL MYOGENESIS.
 AU SONG W K; WANG W; FOSTER R F; BIELSER D A; KAUFMAN S J
 JS DEP. CELL STRUCTURAL BIOL., UNIV. ILLINOIS, URBANA, ILL. 61801.
 SC J CELL BIOL. (1992) 117 (3), 643-657.
 CODEN: JCLB33. ISSN: 0021-9526.
 ES BA; OLD
 LA English
 AB H36 is a 120,000-D membrane glycoprotein that is expressed during the differentiation of skeletal muscle. H36 cDNA clones were isolated from a lambda UniZapNR rat myotube cDNA library and sequenced. The deduced amino acid sequence demonstrates that H36 is a novel **integrin alpha** chain that shares extensive homology with other **alpha integrins** that includes: (a) the CFFKR sequence found in all **alpha integrins**; (b) a single membrane spanning region; (c) conservation of 16 of 22 cysteines; and (d) a protease cleavage site found in the non-I region **integrin alpha** chains. The cytoplasmic domain of H36 is unique and additional regions of nonhomology further indicate H36 is distinct from all other **alpha** chains. In keeping with current nomenclature we designate this **alpha** chain **.alpha.7**. Northern blots demonstrate that expression of H36-**.alpha.7** mRNA is regulated both early in the development of the myogenic lineage and later, during terminal differentiation. Detection of H36-**.alpha.7** mRNA coincides with conversion of H36- myogenic precursor cells to H36+ cells. H36-**.alpha.7** mRNA is present in replicating myoblasts; expression increases upon terminal differentiation and is markedly reduced in developmentally defective myoblasts. In addition, H36-**.alpha.7** mRNA is not detected in C3H10T1/2 cells. It is in myotubes derived from myoblasts obtained by treatment of 10T1/2 cells with azacytidine or transfection with MRF4. Immunoblots and immunofluorescence demonstrate that the H36-**.alpha.7** chain is associated with **integrin .beta.1**. Affinity chromatography demonstrates that H36-**.alpha.7** **.beta.1** selectively binds to laminin. The expression of H36-**.alpha.7** on secondary myoblasts during the development of the limb in vivo corresponds with the appearance of laminin in the limb, with the responsiveness of secondary myoblast proliferation to laminin, and with the onset of increased muscle mass, suggesting that H36-**.alpha.7** modulates this stage in limb development. We conclude that H36-**.alpha.7** is a novel **alpha integrin** laminin binding protein whose expression is developmentally regulated during skeletal myogenesis.
 CC Cytology and Cytochemistry - Animal *02506
 Genetics and Cytogenetics - Animal *03506
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Muscle - Physiology and Biochemistry *17504
 Developmental Biology - Embryology - Morphogenesis, General *25518
 EC Muridae #6375
 IT Miscellaneous Descriptors
 RAT LAMININ AMINO ACID SEQUENCE MOLECULAR SEQUENCE DATA
 EN 1992-07-01, 00701-42-01 INTEGRIN

== file headline

FILE 'HEADLINE' ENTERED AT 11:09:45 ON 13 MAY 2003

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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163 ANSWER 1 OF 45 MEDLINE
AN 2703204286 IN-PROCESS
DN 2.610054 PubMed ID: 12670877
TI Constitutive properties, not molecular adaptations, mediate extraocular muscle sparing in dystrophic mdx mice.
AU Porter John L; Merriam Anita P; Khanna Sangeeta; Andrade Francisco H; Richmonds Chelliah P; Leahy Patrick; Cheng Georgiana; Karathanasis Paraskevi; Zhou Xiaohua; Kusner Linda L; Adams Marvin E; Willem Michael; Mayer Ulrike; Faminski Henry J
CS Department of Ophthalmology, Case Western Reserve University and The Research Institute of University Hospitals of Cleveland, 11100 Euclid Ave., Cleveland, Ohio 44106-5068, USA.. jdp7@po.cwru.edu
SO PASEB JOURNAL, (2003 May) 17 (3) 893-5.
Journal code: 8604484. ISSN: 1530-6860.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STM: 20030502
Last Updated in STM: 20030502
AB Extraocular muscle (EOM) is spared in Duchenne **muscular dystrophy**. Here, we tested putative EOM sparing mechanisms predicted from existing dystrophinopathy models. Data show that mdx mouse EOM contains dystrophin-glycoprotein complex (DGC)-competent and DGC-deficient myofibers distributed in a fiber type-specific pattern. Up-regulation of a dystrophin homologue, utrophin, mediates selective DGC retention. Counter to the IGC mechanical hypothesis, an intact DGC is not a precondition for EOM sarcolemmal integrity, and active adaptation at the level of calcium homeostasis is not mechanistic in protection. A partial, fiber type-specific retention of antiischemic nitric oxide to vascular smooth muscle signaling is not a factor in EOM sparing, because mice deficient in dystrophin and alpha-syntrophin, which localizes neuronal nitric oxide synthase to the sarcolemma, have normal EOMs. Moreover, an alternative transmembrane protein, **alpha7beta1 integrin**, does not appear to substitute for the DGC in EOM. Finally, genome-wide expression profiling showed that EOM does not actively adapt to dystrophinopathy but identified candidate genes for the constitutive protection of mdx EOM. Taken together, data emphasize the conditional nature of dystrophinopathy and the potential importance of nonmechanical DGC roles and support the hypothesis that broad, constitutive structural cell signaling, and/or biochemical differences between EOM and other skeletal muscles are determinants of differential disease responsiveness.

163 ANSWER 2 OF 45 MEDLINE
AN 2703174122 IN-PROCESS
DN 22679929 PubMed ID: 12691739
TI Involvement of **alpha7beta1 integrin** in the conditioning-lesion effect on sensory axon regeneration.
AU Ekstrom Per A P; Mayer Ulrike; Panjwani Aliza; Pountney David; Pinney John; Torge David A
CS Department of Animal Physiology, University of Lund, Helsingavagen 3B, SE-223 62, Lund, Sweden.

- 20 MOLECULAR AND CELLULAR NEUROSCIENCES, (2003 Mar 12) 3: 483-95.
 Journal code: 0969-9961. ISSN: 1044-7431.
 NY United States
 TI Journal; Article; (JOURNAL ARTICLE)
 LI English
 FS IN-PROCESS; NONINDEXED; Priority Journals
 ED Entered STN: 20030416
 Last Updated on STN: 20030416
 AB Conditioning lesions of peripheral nerves improve axonal regeneration after injury and involve changes in expression of proteins required for axonal growth. **Integrin alpha7beta1** expression in motor and sensory neurons increases following nerve lesions and motor axon regeneration is impaired in **alpha7 integrin** KO mice (G. Neurosci. 20, 1822-1830). To investigate the role of **alpha7beta1 integrin** in sensory axon regeneration, dorsal root ganglia of adult mice were cultured in gels of laminin-rich extracellular matrix (Matrigel) or collagen. Normal dorsal root ganglia in Matrigel or collagen supplemented with laminin showed spontaneous axonal outgrowth, which was greatly increased in conditioned preparations, but only in the presence of laminin. Conditioned dorsal root ganglia from normal mice cultured with a blocking antibody to **beta1 integrin** and from **alpha7 integrin** KO mice showed reduced axonal growth in both Matrigel- and laminin-supplemented collagen gels. Enhanced axonal regeneration after conditioning lesions therefore involves increased responsiveness to laminin and **integrin alpha7beta1** expression.
- L83 ANSWER 3 OF 43 MEELINE
 AN 2003116386 IN-PROCESS
 DN 22476683 PubMed ID: 12588796
 TI Defective **integrin** switch and matrix composition at **alpha 7**-deficient myotendinous junctions precede the onset of **muscular dystrophy** in mice.
 AU Nawrotsky Ralph; Willem Michael; Miosge Nicolai; Brinkmeier Heinrich; Mayer Ulrike
 CS Max-Planck-Institute for Biochemistry, 82152 Martinsried, Germany.
 SO HUMAN MOLECULAR GENETICS, (2003 Mar 1) 12 (5) 483-95.
 Journal code: 9208955. ISSN: 0964-6906.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS IN-PROCESS; NONINDEXED; Priority Journals
 ED Entered STN: 20030313
 Last Updated on STN: 20030313
 AB Force transmission at the myotendinous junction requires a strong link between the muscle cytoskeleton and the extracellular matrix. At the adult junction, two splice variants of the laminin-binding **integrins**, **alpha7Abeta1D** and **alpha7Bbeta1D**, are highly enriched. The **alpha7** subunits are critical for the integrity of the junctional sarcolemma because **integrin alpha7**-deficient mice develop **muscular dystrophy**, primarily affecting this site of the muscle. Here, we report that **beta1D integrin** coimmunoprecipitates and colocalizes with the **alpha8** subunit at **alpha7**-deficient junctions, but does not associate with **alpha8**, **alpha4** or **alpha5 integrins**. By immunogold labelling we show that the basement membranes of **integrin alpha7**-deficient muscles recruit abnormally high levels of fibronectin, the ligand of **alpha8beta1D**. Finally, we demonstrate that **alpha8beta1D** is down-regulated at the normal postnatal junction and is displaced by **alpha7beta1D**. These results suggest that the **alpha7** subunit is implicated in the down-regulation of **alpha8beta1D** and in the removal of fibronectin from the maturing myotendinous junction, thus providing an **alpha7beta1D**

-based link to laminin. We propose that the persistence of alpha5beta1 in **alpha7**-deficient mice is not compatible with normal muscle function and leads to muscle wasting.

153 ANSWER 4 OF 45 MEDLINE
 AN 2003113827 MEDLINE
 EN 22516254 PubMed ID: 12629182
 TI Sensory neuron subtypes have unique substratum preference and receptor expression before target innervation.
 AU Guan Wei; Puthenveedu Manojkumar A; Condie Maureen L
 CS Department of Neurobiology and Anatomy, University of Utah, School of Medicine, Salt Lake City, Utah 84132-8401, USA.
 NC R01 NS38138 (NINDS)
 SO JOURNAL OF NEUROSCIENCE, (2003 Mar 1) 23 (5) 1781-91.
 Journal code: 9102140. ISSN: 1529-2401.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 201303
 ED Entered STN: 20030312
 Last Updated on STN: 20030325
 Entered Medline: 20030324
 AB The factors controlling the specification and subsequent differentiation of sensory neurons are poorly understood. Data from embryological manipulations suggest that either sensory neuron fates are specified by the targets they encounter or sensory neurons are considerably more "plastic" with respect to specification than are neurons of the CNS. The prevailing view that sensory neurons are specified late in development is not consistent, however, with the directed outgrowth of sensory neurons to their targets and the characteristic spatial distribution of sensory neuron fates within the peripheral ganglia. To address when in development different classes of sensory neurons can first be distinguished, we investigated the interactions of early dorsal root ganglia neurons with the extracellular matrix before neurite outgrowth to targets. We found that subclasses of sensory neurons in early dorsal root ganglia show different patterns of neurite outgrowth and **integrin** expression that are predictive of their fates. In the absence of neurotrophins, presumptive proprioceptive neurons extend neurites robustly on both laminin and fibronectin, whereas presumptive cutaneous neurons show a strong preference for laminin. Cutaneous afferents that have innervated targets show a similar strong preference for laminin and show higher levels of **integrin alpha7beta1** than do proprioceptive neurons. Finally, presumptive proprioceptive neurons express fibronectin receptors, **integrin alpha8beta1**, **alpha4beta1**, and **alpha5beta1**, at higher levels than do presumptive cutaneous neurons. Our results indicate that subtypes of sensory neurons have unique patterns of neurite outgrowth and receptor expression before target innervation.
 CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
 Cell Differentiation: DE, drug effects
 Cell Differentiation: PH, physiology
 Chick Embryo
 Extracellular Matrix: ME, metabolism
 Fibronectins: ME, metabolism
 Fibronectins: PD, pharmacology
 Ganglia, Spinal: CY, cytology
 Ganglia, Spinal: EM, embryology
 Ganglia, Spinal: ME, metabolism
 Integrins: BI, biosynthesis
 Integrins: GE, genetics
 Laminin: ME, metabolism
 Laminin: PD, pharmacology

Nerve Growth Factor: EC, pharmacology
 Neurites: DE, drug effects
 Neurites: EH, physiology
 *Neurons, Afferent: CL, classification
 *Neurons, Afferent: CY, cytology
 Neurons, Afferent: DE, drug effects
 Neurons, Afferent: ME, metabolism
 Neurotrophin 3: PD, pharmacology
 RNA, Messenger: BI, biosynthesis
 Receptor, trkA: BI, biosynthesis
 Receptor, trkC: BI, biosynthesis
 *Receptors, Cell Surface: BI, biosynthesis
 *Receptors, Fibronectin: BI, biosynthesis
 RN 9001-01-4 (Nerve Growth Factor)
 CN 0 (Fibronectins); 0 (**Integrins**); 0 (Laminin); 0 (Neurotrophin 3); 0 (RNA, Messenger); 0 (Receptors, Cell Surface); 0 (Receptors, Fibronectin); EC 2.7.1.112 (Receptor, trkA); EC 2.7.1.112 (Receptor, trkC)

L83 ANSWER 5 OF 45 MEDLINE
 AN 200245481 MEDLINE
 DN 22201697 PubMed ID: 12213731
 TI Expression of **alpha7beta1 integrin** splicing variants during skeletal muscle regeneration.
 AU Kaariainen Minna; Nissinen Liisa; Kaufman Stephen; Sonnenberg Arnoud; Jarvinen Markku; Heino Jyrki; Kalimo Hannu
 CS Medical School and the Institute of Medical Technology, University of Tampere, Finland.
 SO AMERICAN JOURNAL OF PATHOLOGY, (2002 Sep) 161 (3) 1023-31.
 Journal code: C:70502. ISSN: 0002-9440.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM L00209
 ED Entered STN: 20020906
 Last Updated on STN: 20020928
 Entered Medline: 20020927

AB **Integrin alpha7beta1** is a laminin receptor, both subunits of which have alternatively spliced, developmentally regulated variants. In skeletal muscle **beta1** has two major splice variants of the intracellular domain (**beta1A** and **beta1D**). **alpha7X1** and **alpha7X2** represent variants of the **alpha7** ectodomain, whereas **alpha7A** and **alpha7B** are variants of the intracellular domain. Previously we showed that during early regeneration after transection injury of muscle **alpha7 integrin** mediates dynamic adhesion of myofibers along their lateral aspects to the extracellular matrix. Stable attachment of myofibers to the extracellular matrix occurs during the third week after injury, when new myotendinous junctions develop at the ends of the regenerating myofibers. Now we have analyzed the relative expression of **beta1A/beta1D** and **alpha7A/alpha7B** and **alpha7X1** and **alpha7X2** isoforms during regeneration for 2 to 56 days after transection of rat soleus muscle using reverse transcriptase-polymerase chain reaction and immunohistochemistry. During early regeneration **beta1A** was the predominant isoform in both the muscle and spinal tissue. Expression of muscle-specific **beta1D** was detected in regenerating myofibers from day 4 onwards, i.e., when myogenic protein activity began to decrease, and it became more abundant with the progression of regeneration. **alpha7B** isoform predominated on day 2. Thereafter, the relative expression of **alpha7A transcripts** increased until day 7 with the concomitant appearance of **alpha7A** immunoreactivity on regenerating myofibers. Finally, **alpha7B** again became the predominant variant in highly regenerated

myofibers. Similarly as in the controls, **alpha7X1** and **alpha7X2** isoforms were both expressed throughout the regeneration with a peak in **alpha7X1** expression on day 4 coinciding with the dynamic adhesion stage. The results suggest that during regeneration of skeletal muscle the splicing of **beta1** and **alpha7** integrin subunits is regulated according to functional requirements. **alpha7A** and **alpha7X1** appear to have a specific role during the dynamic phase of adhesion, whereas **alpha7B**, **alpha7X2**, and **beta1D** predominate during stable adhesion.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't

*Integrins: BI, biosynthesis

*Integrins: GE, genetics

Muscle, Skeletal: ME, metabolism

*Muscle, Skeletal: PH, physiology

Protein Structure, Tertiary: GE, genetics

RNA Splicing

Rats

Rats, Sprague-Dawley

*Regeneration: PH, physiology

CN 0 (Integrins); 0 (integrin alpha7beta1)

183 ANSWER 6 OF 45 MEDLINE

AN 2102315192 MEDLINE

DN 21052264 PubMed II: 12157917

TI Integrin alpha 7 beta 1

in muscular dystrophy/myopathy of unknown etiology.

AU Pegoraro Elena; Depollart Fulvio; Prandini Paola; Marin Alessandra; Fanin Marina; Trevisan Carlo P; El-Messlemani Abdul Hassib; Tarone Guido; Engvall Eva; Hoffman Eric P; Angelini Corrado

CS Neuromuscular Center, Department of Neurological and Psychiatric Sciences, University of Padova, Padova, Italy.. elena.pegoraro@unipd.it

SO AMERICAN JOURNAL OF PATHOLOGY, (2002 Jun) 160 (6) 2135-43.

Journal code: 0371502. ISSN: 0002-9440.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200207

ED Entered STN: 20020611

Last Updated on STN: 20020809

Entered Medline: 20020715

AB To investigate the role of integrin alpha 7

in muscle pathology, we used a "candidate gene" approach in a large cohort of muscular dystrophy/myopathy patients. Antibodies

against the intracellular domain of the integrin alpha

7A and alpha 7B were used to stain muscle

biopsies from 210 patients with muscular

dystrophy/myopathy of unknown etiology. Levels of alpha

7A and alpha 7B integrin were found

to be decreased in 35 of 210 patients (approximately 17%). In six of these patients no integrin alpha 7B was

detected. Screening for alpha 7B mutation

in 35 of 35 patients detected only one integrin alpha

7 missense mutation. The mutation on the second allele was not

found in a patient presenting with a congenital muscular

dystrophy-like phenotype. No integrin alpha

7 gene mutations were identified in all of the other patients

showing integrin alpha 7 deficiency. In the

process of mutation analysis, we identified a novel integrin

alpha 7 isoform presenting 71-kb deletion. This isoform

results from a partial deletion of exon 11 due to the use of a cryptic splice site generated by a G to A missense mutation at nucleotide position

2044 in **integrin alpha 7 cDNA**. This spliced isoform is present in about 11 of the chromosomes studied. We conclude that **secondary integrin alpha 7 deficiency** is rather common in **muscular dystrophy myopathy** of unknown etiology, emphasizing the multiple mechanisms that may modulate **integrin** function and stability.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Alternative Splicing

Biopsy

Child

Child, Preschool

Down-Regulation

Fluorescent Antibody Technique

Infant

Integrins: DF, deficiency

Integrins: GE, genetics

***Integrins**: PH, physiology

Muscles: PA, pathology

Muscular Diseases: PA, pathology

*Muscular Diseases: PP, physiopathology

Muscular Dystrophies: PA, pathology

***Muscular Dystrophies**: PP, physiopathology

Mutation

Mutation, Missense

Oligonucleotide Array Sequence Analysis

Polymorphism, Single-Stranded Conformational

RNA, Messenger: ME, metabolism

Restriction Mapping

Reverse Transcriptase Polymerase Chain Reaction

CN 0 **Integrins**; C (RNA, Messenger); 0 (**integrin alpha7beta1**)

L83 ANSWER 7 CF 45 MEDLINE

AN 2002210291 MEDLINE

DN 21881641 PubMed ID: 11884516

TI Association of the tetraspanin CD151 with the laminin-binding **integrins** alpha3beta1, alpha6beta1, alpha6beta4 and **alpha7beta1** in cells in culture and in vivo.

CM Erratum in: J Cell Sci 2002 Jun 15;115(Pt 12):2615

AU Sterk Lotus M T; Geuijen Cecile A W; van den Berg Jose G; Claessen Nike; Weening Jan J; Sonnenberg Arnaud

CS Division of Cell Biology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.

SO JOURNAL OF CELL SCIENCE, (2002 Mar 15) 115 (Pt 6) 1161-73.

Journal code: 0022457. ISSN: 0021-9533.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

PS Priority Journals

EM 200210

ED Entered STN: 20020412

Last Updated on STN: 20021217

Entered Medline: 20011109

AB CD151 is a cell surface protein that belongs to the tetraspanin superfamily. It forms complexes with the laminin-binding **integrins** alpha3beta1, alpha6beta1 and alpha6beta4 and is redistributed with these **integrins** in many tissues at sites of cell-matrix interactions. In this study we show that CD151 can also form stable complexes with the laminin-binding **integrin** **alpha7beta1**. The strength of this interaction is comparable to that between CD151 and alpha3beta1. Complexes of alpha6beta1, alpha6beta4 and **alpha7beta1** with CD151 are equally well formed with all splice variants of the alpha3, alpha6 and **alpha7** subunits, and

Complex formation is not affected by mutations that prevent the cleavage of the **integrin** alpha subunit. Like the expression of alpha3beta1 and alpha6beta1, expression of **alpha7beta1** in R661 cells results in increased levels of CD151 at its surface. Two non-integrin laminin receptors, cystroglycan and the polypeptide on which the Lutheran blood group antigens are expressed, are also often colocalized with CD151, but no association with CD151-alpha3beta1 complexes was found with biochemical analysis. The anti-CD151 antibody TS151R detects an epitope at a site at which CD151 interacts with **integrins**, and therefore it cannot react with CD151 when it is bound to an **integrin**. Comparison of the staining patterns produced by TS151R with that by of an anti-CD151 antibody recognizing an epitope outside the binding site (P48) revealed that most tissues expressing one or more laminin-binding **integrins** reacted with P48 but not with TS151R. However, smooth muscle cells that express **alpha7beta1** and renal tubular epithelial cells that express alpha6beta1 were stained equally well by TS151R and P48. These results suggest that the interactions between CD151 and laminin-binding **integrins** are subject to cell-type-specific regulation.

CT Check Tags: Human; Support, Non-U.S. Gov't

Antibodies, Monoclonal: IM, immunology

Antigens, CD: IM, immunology

*Antigens, CD: ME, metabolism

*Antigens, Surface: ME, metabolism

Cells, Cultured

Cytoskeletal Proteins: PH, physiology

Epitopes: IM, immunology

Integrin alpha3beta1

Integrin alpha6beta1

Integrin alpha6beta4

***Integrins: ME, metabolism**

R562 Cells

Kidney Glomerulus: ME, metabolism

Kidney Glomerulus: UL, ultrastructure

Kidney Tubules: CY, cytology

Kidney Tubules: ME, metabolism

Kidney Tubules: UL, ultrastructure

Lutheran Blood-Group System: PH, physiology

Membrane Glycoproteins: PH, physiology

Muscles: AH, anatomy & histology

Muscles: CY, cytology

Muscles: ME, metabolism

Muscles: UL, ultrastructure

Receptors, Laminin: ME, metabolism

Skin: CY, cytology

Skin: ME, metabolism

Skin: UL, ultrastructure

RN 146888-27-9 (43-156K dystrophin-associated glycoprotein)

CU 0 (Antibodies, Monoclonal); 0 (Antigens, CD); 0 (Antigens, Surface); 1 (CD151 antigen, human); 0 (Cytoskeletal Proteins); 0 (Epitopes); 1

Integrin alpha3beta1; 1 **Integrin alpha6beta1**;

Integrin alpha6beta4; 0 **Integrins**; 0 (Lutheran

Blood-Group System); 1 Membrane Glycoproteins; 1 Receptors, Laminin; 1 **integrin alpha7beta1**

L60 ANSWER 4 OF 48 MEDLINE

RN 211212789 MEDLINE

IN 211212789 PubMed ID: 11744715

TI Alternative splice variants of alpha 7 beta

1 **integrin** selectively recognize different laminin isoforms.

AU von der Mark Helga; Williams Inka; Wendler Olaf; Strickin Lydia; von der Mark Klaus; Paschke Ernst

CC Friedrich-Alexander-Universität Erlangen-Nürnberg, Nikolaus-Fischer-
 Centrum für Molekulare Medizin, Department of Experimental Medicine I,
 91054 Erlangen, Germany.
 SI JOURNAL OF BIOLOGICAL CHEMISTRY, 2002 Feb 15; 277(4):2011-6.
 Journal code: 0021-9212. ISSN: 0021-9212.
 CY United States
 DT Journal; Article; [JOURNAL ARTICLE]
 LA English
 FS Priority Journals
 EM 200104
 ED Entered STN: 20020227
 Last Updated on STN: 20030105
 Entered Medline: 20010424
 AB The **integrin alpha(7)beta(1)**
 1 occurs in several cytoplasmic **alpha(7A)**,
alpha(7B) and extracellular splice variants
alpha(7X1), **alpha(7X2)**, which are differentially expressed during
 development of skeletal and heart muscle. The extracellular variants
 result from the alternative splicing of exons X1 and X2, corresponding to
 a segment within the putative ligand binding domain. To study the
 specificity and affinity of the X1/X2 variants to different laminin
 isoforms, soluble **alpha(7)beta(1)**
 complexes were prepared by recombinant coexpression of the extracellular
 domains of the alpha- and beta-subunits. The binding of these complexes
 to purified ligands was measured by solid phase binding assays.
 Surprisingly, the alternative splice variants revealed different and
 specific affinities to different laminin isoforms. While the **alpha(7X2)**
 variant bound much more strongly to laminin-1 than the **alpha(7X1)** variant,
 the latter showed a high affinity binding to laminins-8 and -10/11.
 Laminin-2, the major laminin isoform in skeletal muscle, was recognized by
 both variants, whereas none of the two variants were able to interact with
 laminin-5. A specific blocking antibody inhibited the binding of both
 variants to all laminins tested, indicating the involvement of common
 epitopes in **alpha(7X1)beta(1)** and **alpha(7X2)**
beta(1). Because laminin-8 and -10/11 as well as
alpha(7X1) are expressed in developing skeletal and cardiac muscle, these
 findings suggest that **alpha(7X1)beta(1)** may represent
 a physiological receptor with novel specificities for laminin-8 and -10.
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
 *Alternative Splicing
 Binding Sites
 Dimerization
 *Integrins: GE, genetics
 *Integrins: ME, metabolism
 Kinetics
 *Laminin: ME, metabolism
 Mice
 Myocardium: ME, metabolism
 Protein Isoforms: ME, metabolism
 Protein Subunits
 Recombinant Proteins: ME, metabolism
 Tumor Cells, Cultured
 *Variation: Genetics
 CN **Integrins** ; 1 **Laminin** ; 1 **Protein Isoforms** ; 1 **Protein**
Subunits ; 1 **Recombinant Proteins** ; 1 **integrin**
alpha7beta1 ; 1 **Laminin 1**
 LA ANSWER 2 OF 48 MEDLINE
 AN 2001041152 MEDLINE
 IN 20010424 PubMed ID: 11604741
 TI The role of **integrins** in human embryo implantation.
 AU Merviel G; Chailion J C; Carbillon L; Fournet J M; Yeak J
 SE Service de Gynécologie-Obstétrique et Médecine de la Reproduction, Hôpital

- Tenon, Paris, France.. philippe.merviel@tenon.ap-hop-paris.fr
 FETAL DIAGNOSIS AND THERAPY, 2001 Nov-Dec; 10(4):364-71. Ref: 45
 Journal code: 2127463. ISSN: 1113-3657.
 CY Switzerland
 JT Journal; Article; [JOURNAL ARTICLE]
 General Review; [REVIEW]
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 200201
 ED Entered STN: 20011107
 Last Updated on STN: 20020125
 Entered Medline: 20020116
 AB **Integrins** are adhesion molecules present in endometrial, decidua, and extravillous cytotrophoblast (EVT) cells. They participate in cell-cell adhesion as well as in adhesion between cells and components of the extracellular matrix, and they play an important role in the endometrial phenotype change that occurs during the secretory phase, the first stage of implantation. At the beginning of pregnancy, the change in **integrin** expression is synchronized with the trophoblast attachment (embryo-endometrium interactions with **integrins** alpha(v)beta3, alpha4beta1, alpha6beta1, and **alpha7beta1**) and the embryo's invasion of the decidua (**integrins** alpha6beta4-->alpha6beta1-->alpha1beta1-->alpha4beta1 switch from proliferative to endovascular EVT). Several diseases, including preeclampsia, intrauterine growth retardation caused by vascular problems and defective luteal phases, may be explained by anomalies in **integrin** patterns.
 Copyright 2001 S. Karger AG, Basel
 CT Check Tags: Female; Human
 Cell Adhesion Molecules: FH, physiology
 *Embryo Implantation: PH, physiology
 Endometriosis
 Infertility, Female
 *Integrins: PH, physiology
 Pre-Eclampsia
 Pregnancy
 Trophoblasts: CY, cytology
 Trophoblasts: PH, physiology
 CN 0 (Cell Adhesion Molecules); 0 (**Integrins**)
 L83 ANSWER 10 OF 45 MEDLINE
 AN 2001516591 MEDLINE
 DN 21234604 PubMed ID: 11329371
 TI HEMCAM/CD146 downregulates cell surface expression of **beta1 integrins**.
 AU Alais C; Allioi N; Pujades C; Duband J L; Vainio O; Imhof B A; Dunon D
 CC UMR-CNRS 7622, Universite Pierre et Marie Curie, Paris, France.
 SO JOURNAL OF CELL SCIENCE, (2001 May) 114 (Pt 10):1647-54.
 Journal code: 0022457. ISSN: 0021-9533.
 CY England; United Kingdom
 JT Journal; Article; [JOURNAL ARTICLE]
 LA English
 FS Priority Journals
 EM 200110
 ED Entered STN: 20011024
 Last Updated on STN: 20011024
 Entered Medline: 20011024
 AB HEMCAM/glypican, an immunoglobulin superfamily protein, is involved in homophilic and heterophilic adhesion. It interacts with NFP, neurite outgrowth factor, a molecule of the laminin family. Alternative splicing leads to mRNAs coding for HEMCAM with a short HEMCAM-s or a long cytoplasmic tail HEMCAM-l. To investigate the cellular function of

these two variants, we stably transfected murine fibroblasts with either form of HEMCAM. Expression of each isoform of this protein in L cells delayed proliferation and modified their adhesion properties to purified extracellular matrix proteins. Expression of either HEMCAM-6 or HEMCAM-1 inhibited **integrin**-dependent adhesion and spreading of fibroblasts to laminin 1, showing that this phenomenon did not depend on the cytoplasmic region. By contrast, L-cell adhesion and spreading to fibronectin depended on the HEMCAM isoform expressed. Flow cytometry and immunoprecipitation studies revealed that the expression of HEMCAM downregulated expression of the laminin-binding **integrins** alpha3beta1, alpha6beta1 and **alpha7beta1**, and fibronectin receptor alpha5beta1 from the cell surface. Semi-quantitative PCR and northern blot experiments showed that the expression of alpha6beta1 **integrin** modified by HEMCAM occurred at a **translation** or maturation level. Thus, our data demonstrate that HEMCAM regulates fibroblast adhesion by controlling **beta1 integrin** expression.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't

*Antigens, CD29: GE, genetics

*Antigens, CD29: ME, metabolism

Antigens, Surface: GE, genetics

Antigens, Surface: ME, metabolism

Cell Adhesion: PH, physiology

*Cell Adhesion Molecules: GE, genetics

*Cell Adhesion Molecules: ME, metabolism

Cell Division: PH, physiology

Cell Movement: PH, physiology

Cells, Cultured

Chick Embryo

Down-Regulation: PH, physiology

Fibroblasts: CY, cytology

Fibroblasts: ME, metabolism

Flow Cytometry

Gene Expression Regulation, Developmental

Integrin alpha6beta1

Integrins: GE, genetics

Integrins: ME, metabolism

Membrane Proteins: GE, genetics

Membrane Proteins: ME, metabolism

Nice

Molecular Sequence Data

RNA, Messenger: AN, analysis

Sequence Homology, Amino Acid

Transcription, Genetic: PH, physiology

Transfection

CN 0 (Antigens, CD29); 0 (Antigens, Surface); 0 (Cell Adhesion Molecules); 0 (HEMCA protein); 0 (**Integrin alpha6beta1**); 0 **Integrins**; 0 (MCAM protein, human); 0 (Membrane Proteins); 0 (RNA, Messenger).

193 ANSWER 11 OF 45 MEDLINE

AN 2001268240 MEDLINE

EN 21259472 PubMed ID: 11361006

TI Transfection of MCF-7 carcinoma cells with human **integrin alpha7** cDNA promotes adhesion to laminin.

AF Vassiliadis I B; Yao C C; Chen Y; Dicker E L; Tsiftoglou A C; Kramer E B
DE Department of Hematology, University of California at San Francisco, 24143-0112, USA.

JO ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, 2001 Jan 1; 390: 1-10-10.
Journal Code: 0003-9825. ISSN: 0003-9825.

NY United States

IT Journal; Article; JOURNAL ARTICLE

LA English

EO Priority Journals

CS GENBANK-AF071131
 EX 200106
 FI Entered STN: 20010625
 Last Updated on STN: 20010625
 Entered Medline: 20010621

AB The laminin-binding **alpha7beta1 integrin** receptor is highly expressed by skeletal and cardiac muscles, and has been suggested to be a crucial molecule during myogenic cell migration and differentiation. Absence of **integrin alpha7** subunit contributes to a form of **muscular dystrophy** in **integrin alpha7** null mice, whereas specific mutations in the **alpha7** gene are associated in humans with congenital myopathy. To examine in more detail the potential role of **integrin alpha7** in human-related muscular disorders, we cloned **alpha7** cDNA by RT-PCR from human skeletal muscle mRNA and then expressed the full-length human **integrin alpha7** cDNA by transfection in several cell lines including MCF-7, COS-7, and NIH3T3 cells. The isolated cDNA corresponds to the human **alpha7X2B** alternative splice form. Expression of human **alpha7** was further confirmed by transfection of chimeric human-mouse **alpha7** cDNA constructs. To demonstrate the functionality of expressed human **alpha7**, adhesion experiments with transfected MCF-7 cells have confirmed the specific binding of human **alpha7** to laminin. In addition, mouse polyclonal and monoclonal antibodies were generated against the extracellular domain of human **alpha7** and used to analyze by flow cytometry MCF-7 and NIH3T3 cells transfected with the full-length of human **alpha7** cDNA. These results show for the first time the exogenous expression of functional full-length human **alpha7** cDNA, as well as the development of monoclonal antibodies against the human **alpha7** extracellular domain. Antibodies developed will be useful for further analysis of human disorders involving **alpha7** dysfunction and facilitate isolation of muscle stem cells (satellite cells) and thereby expand the opportunities for genetically modified transplantation treatment of human disease.

CT Check Tags: Animal; Human
 3T3 Cells

Alternative Splicing
 Antibodies, Monoclonal: ME, metabolism
 *Antigens, CD: GE, genetics
 Antigens, CD: ME, metabolism
 Biotin: ME, metabolism
 Blotting, Western
 *Breast Neoplasms: ME, metabolism
 *Breast Neoplasms: PA, pathology
 COS Cells
 Cell Adhesion
 Cell Line
 Cell Separation
 Cloning, Molecular
 DNA, Complementary: ME, metabolism
 Flow Cytometry
 Immunohistochemistry
 *Laminin: ME, metabolism
 Mice
 Molecular Sequence Data
 Muscle, Skeletal: ME, metabolism
 Precipitin Tests
 Protein Structure, Tertiary
 RNA, Messenger: ME, metabolism
 Reverse Transcriptase Polymerase Chain Reaction
 Transfection
 Tumor Cells, Cultured

EN 88-45-5 Biotin
 CN 1 Antibodies, Monoclonal ; 1 Antigens, CD ; 1 DNA, Complementary ;
 1 ITGA7 protein, human ; 1 Laminin ; 1 RNA, Messenger ; 1 Laminin 1

L63 ANSWER 12 OF 45 MEDLINE
 AN 2001253114 MEDLINE
 CN 21220787 PubMed ID: 11319864
 TI Laminin-induced change in conformation of preexisting **alpha7beta1 integrin** signals secondary myofiber formation.
 AU Blanco-Bose W E; Blau H M
 OS Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, California 94305-5175, USA.
 NC A509521 (NIA)
 CA59717 (NCI)
 H118179 (NIDHD)
 SO DEVELOPMENTAL BIOLOGY, (2001 May 1) 233 (1): 149-60.
 J urnal code: 0372762. ISSN: 0012-1606.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200105
 ED Entered STM: 20010604
 Last Updated on STM: 20010604
 Entered Medline: 20010531

AB Two distinct populations of myoblasts, distinguishable by **alpha7 integrin** expression have been hypothesized to give rise to two phases of myofiber formation in embryonic limb development. We show here that **alpha7 integrin** is detectable far earlier than previously reported on both "primary" and "secondary" lineage myoblasts and myofibers. An antibody (1211) that recognizes an intracellular epitope allowed detection of **alpha7 integrin** previously missed using an antibody (H36) that recognizes an extracellular epitope. We found that when myoblasts were isolated and cultured from different developmental stages, H36 only detected **alpha7 integrin** that was in direct contact with its ligand, laminin. Moreover, **alpha7 integrin** detection by H36 was reversible and highly localized to subcellular points of contact between myoblasts and laminin-coated 2.8-microm microspheres. Prior to secondary myofiber formation in limb embryogenesis, laminin was present but not in close proximity to clusters of primary myofibers that expressed **alpha7 integrin** detected by antibody 1211 using deconvolution microscopy. These results suggest that the timing of the interaction of preexisting **alpha7 integrin** with its ligand, laminin, is a major determinant of allosteric changes that result in an activated form of **alpha7 integrin** capable of transducing signals from the extracellular matrix commensurate with secondary myofiber formation.
 Copyright 2001 Academic Press.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
 Animals, Newborn
 Antibody Specificity
 Antigens, CD: 3E, genetics
 Antigens, CD: IM, immunology
 Cell Compartmentation
 Cell Differentiation
 Cells, Cultured
 Collagen: ME, metabolism
 Hindlimb: CY, cytology
 Integrins: CH, chemistry
 *Integrins: ME, metabolism
 *Laminin: ME, metabolism
 *Muscle Fibers: CY, cytology

*Muscle, Skeletal: CY, cytology
 *Protein Conformation
 RNA, Messenger
 Rats
 Rats, Sprague-Dawley
 Receptors, Laminin: CH, chemistry
 *Receptors, Laminin: ME, metabolism
 Signal Transduction
 *Stem Cells: CY, cytology
 Tissue Culture

RN 9007-34-5 (Collagen)
 SN 0 (Antigens, CD); 0 (ITGA7 protein, human); 0 (**Integrins**); 0 (Laminin); 0 (RNA, Messenger); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

L83 ANSWER 13 OF 45 MEDLINE
 AN 2001227981 MEDLINE
 DN 21157400 PubMed ID: 11257121
 TI Enhanced expression of the **alpha 7 beta 1 integrin** reduces **muscular dystrophy** and restores viability in dystrophic mice.
 AU Burkin D J; Wallace J Q; Nicol K J; Kaufman D J; Kaufman S J
 CS Department of Cell and Structural Biology, University of Illinois, Urbana, Illinois 61801, USA.
 SO JOURNAL OF CELL BIOLOGY, (2001 Mar 19) 152 (6) 1207-18.
 Journal code: 03759550. ISSN: 0021-9525.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200104
 ED Entered STN: 20010502
 Last Updated on STN: 20010502
 Entered Medline: 20010426

AB Muscle fibers attach to laminin in the basal lamina using two distinct mechanisms: the dystrophin glycoprotein complex and the **alpha 7 beta 1 integrin**. Defects in these linkage systems result in Duchenne **muscular dystrophy** (DMD), **alpha 2 laminin congenital muscular dystrophy**, sarcoglycan-related **muscular dystrophy**, and **alpha 7 integrin congenital muscular dystrophy**. Therefore, the molecular continuity between the extracellular matrix and cell cytoskeleton is essential for the structural and functional integrity of skeletal muscle. To test whether the **alpha 7 beta 1 integrin** can compensate for the absence of dystrophin, we expressed the rat **alpha 7** chain in mdx/utr(-/-) mice that lack both dystrophin and utrophin. These mice develop a severe **muscular dystrophy** highly akin to that in DMD, and they also die prematurely. Using the muscle creatine kinase promoter, expression of the **alpha 7 beta 1 integrin** chain was increased 2.0-2.3-fold in mdx/utr(-/-) mice. Concomitant with the increase in the **alpha 7** chain, its heterodimeric partner, beta 1, was also increased in the transgenic animals. Transgenic expression of the **alpha 7 beta 1 integrin** chain in the mdx/utr(-/-) mice extended their longevity by threefold, reduced myofiber atrophy and the development of muscle disease, and maintained mobility and the structure of the neuromuscular junction. Thus, bolstering **alpha 7 beta 1 integrin**-mediated association of muscle cells with the extracellular matrix alleviates many of the symptoms of disease observed in mdx/utr(-/-) mice and compensates for the absence of the dystrophin- and utrophin-mediated linkage systems. This suggests that enhanced expression of the **alpha 7 beta 1 integrin**

may provide a novel approach to treat IMD and other muscle diseases that arise due to defects in the dystrophin glycoprotein complex. A video that contrasts kyphosis, gait, joint contractures, and mobility in mdx utr - - and alpha 7BM2-mdx utr - - mice can be accessed at <http://www.job.org/cgi/content/full/158/6/1111>.

Check Tags: Animal; Female; Human; Male; Support; Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Blotting, Western

Body Weight

Contracture: PP, physiopathology
Creatine Kinase: GE, genetics
Cytoskeletal Proteins: GE, genetics
Cytoskeletal Proteins: ME, metabolism
Dystrophin: GE, genetics
Dystrophin: ME, metabolism
Hindlimb

Integrins: GE, genetics

***Integrins: ME, metabolism**

Isoenzymes: GE, genetics

Joints

Kyphosis

Magnetic Resonance Imaging

Membrane Proteins: GE, genetics
Membrane Proteins: ME, metabolism

Mice

Mice, Inbred mdx

Mice, Transgenic

Microscopy, Fluorescence

Muscle, Skeletal: PA, pathology

*Muscle, Skeletal: PP, physiopathology

Muscular Dystrophy, Animal: GE, genetics

Muscular Dystrophy, Animal: PA, pathology

Muscular Dystrophy, Animal: PP, physiopathology

Muscular Dystrophy, Duchenne: GE, genetics

Muscular Dystrophy, Duchenne: PA, pathology

***Muscular Dystrophy, Duchenne: PP, physiopathology**

Neuromuscular Junction: UL, ultrastructure

*Promoter Regions (Genetics)

Fats

Receptors, Cholinergic: ME, metabolism

Receptors, Cholinergic: UL, ultrastructure

Survival Rate

Transgenes

CN 0 (Cytoskeletal Proteins); 0 (Dystrophin); 0 (Integrins); 0 (Isoenzymes); 0 (Membrane Proteins); 0 (Receptors, Cholinergic); 0 (cystrophin-related protein); 0 (integrin alpha7beta1); EC 2.7.3.2 (Creatine Kinase); EC 2.7.3.2.- (creatine kinase, MM form).

L83 ANSWER 14 OF 45 MEDLINE

AN 2001009994 MEDLINE

EN 20006592 PubMed ID: 10966444

TI Cell-cell adhesion via the ECM: integrin genetics in fly and worm.

AF Brown N H

AD Wellcome/CRC Institute and Department of Anatomy, University of Cambridge, Tennis Court Rd, CB2 1TP, Cambridge, UK. n.h.brown@cam.ac.uk

SO NATURE BIOLOGY, 2001, Vol 1, No 1, 101-111. Per: 66

Journal code: 09502688. ISSN: 1471-0021.

DE GERMANY: Germany, Federal Republic of

TI Journal; Article; JOURNAL ARTICLE

General Review; REVIEW

REVIEW, TUTORIAL

LA English

EC Priority Journals
 EM 20010
 ED Entered STN: 20010321
 Last Updated on STN: 20010321
 Entered Medline: 20010321
 AB **Integrins** are essential for the development of the two genetically tractable invertebrate model organisms, the nematode worm *Caenorhabditis elegans* and the fruit fly *Drosophila melanogaster*. Just two **integrins** are present in *C. elegans*: one putative RGD binding **integrin** α pat-2 β pat-3, corresponding to *Drosophila* α PS2 β PS and vertebrate α 5 β 1, α 4 β 1 and α 8 β 1, and one putative laminin binding **integrin** α pat-1 β pat-3, corresponding to *Drosophila* α PS1 β PS and vertebrate α 3 β 1, α 6 β 1 and α 7 β 1. In this review, the function of this minimal set of **integrins** during the development of these two invertebrates is compared. Despite the differences in bodyplan and developmental strategy, **integrin** adhesion to the extracellular matrix is required for similar processes: the formation of the link that **translates** muscle contraction into movement of the exoskeleton, cell migration, and morphogenetic interactions between epithelia. Other **integrin** functions, such as regulation of gene expression, have not yet been experimentally demonstrated in both organisms. Additional proteins have been characterised in each organism that are essential for **integrin** function, including extracellular matrix ligands and intracellular interacting proteins, but so far different proteins have been found in the two organisms. This in part represents the fact that the characterisation of the full set of interacting proteins is not complete in either system. However, in other cases different proteins appear to be used for similar functions in the two animals. The continued use of genetic approaches to identify proteins required for **integrin** function in these two model organisms should lead to the identification of the minimal set of conserved components that form **integrin** adhesive structures.
 CT Check Tags: Animal; Human
Caenorhabditis elegans: GE, genetics
 Cell Adhesion
Drosophila melanogaster: PH, physiology
 Extracellular Matrix: ME, metabolism
 Forecasting
 Integrins: CL, classification
 *Integrins: GE, genetics
 Integrins: PH, physiology
 Invertebrates: GE, genetics
 Phenotype
 Vertebrates: GE, genetics
 CN 0 (Integrins); 0 (integrin PS, *Drosophila*); 1 (integrin β pat-3)
 L63 ANSWER 15 OF 45 MEDLINE
 AN 2001496259 MEDLINE
 DN 20012693 PubMed ID: 10910772
 TI Laminin and α 7 β 1 integrin regulate agrin-induced clustering of acetylcholine receptors.
 AU Burkin D J; Kim J E; Gu M; Kaufman J J
 AD Department of Cell and Structural Biology, University of Illinois, Urbana, IL 61801, USA.
 JO JOURNAL OF CELL SCIENCE, 2001 Aug; 113 Pt 16: 2891-90.
 Journal code: 0021-9595, ISSN: 0021-9595.
 CY ENGLAND: United Kingdom
 JT Journal; Article; JOURNAL ARTICLE
 LA English
 FC Priority Journals
 EM 20010

- EI Entered CTN: 0110107
 Last Updated on CTN: 0110107
 Entered Medline: 0110112
- AB The clustering of acetylcholine receptors (AChRs) in the post-synaptic membrane of skeletal muscle is an early developmental event in the formation of the neuromuscular junction. Several studies show that laminin, as well as neural agrin, can induce AChR clustering in C1010 myofibers. We recently showed that specific isoforms of the **alpha7beta1 integrin** (a receptor normally found at neuromuscular junctions) colocalize and physically interact with AChR clusters in a laminin-dependent fashion. In contrast, induction with agrin alone fails to promote localization of the **integrin** with AChR clusters. Together both agrin and laminin enhance the interaction of the **integrin** with AChRs and their aggregation into clusters. To further understand this mechanism we investigated cluster formation and the association of the **alpha7beta1 integrin** and AChR over time following induction with laminin and/or agrin. Our results show that the **alpha7beta1 integrin** associates with AChRs early during the formation of the post-synaptic membrane and that laminin modulates this recruitment. Laminin induces a rapid stable association of the **integrin** and AChRs and this association is independent of clustering. In addition to laminin-1, merosin (laminin-2/4) is present both before and after formation of neuromuscular junctions and also promotes AChR clustering and colocalization with the **integrin** as well as synergism with agrin. Using site directed mutagenesis we demonstrate that a tyrosine residue in the cytoplasmic domain of both (α7A and (α7B chains regulates the localization of the **integrin** with AChR clusters. We also provide evidence that laminin, through its association with the **alpha7beta1 integrin**, reduces by 20-fold the concentration of agrin required to promote AChR clustering and accelerates the formation of clusters. Thus laminin, agrin and the **alpha7beta1 integrin** act in a concerted manner early in the development of the post-synaptic membrane, with laminin priming newly formed myofibers to rapidly and vigorously respond to low concentrations of neural agrin produced by innervating motor neurons.
- CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Agrin: ME, metabolism
 *Agrin: PD, pharmacology
 Cells, Cultured
 Cytoplasm: ME, metabolism
 Fluorescent Antibody Technique
 Immunoblotting
 Integrins: AN, analysis
 *Integrins: ME, metabolism
 Laminin: ME, metabolism
 *Laminin: PD, pharmacology
 Mice
 Muscle Fibers: CH, chemistry
 Muscle Fibers: CY, cytology
 *Muscle Fibers: ME, metabolism
 Neuromuscular Junction: ME, metabolism
 Protein Binding: DE, drug effects
 Receptors, Cholinergic: AN, analysis
 *Receptors, Cholinergic: ME, metabolism
 Tyrosine: ME, metabolism
- AN 01101-40-6 Tyrosine
 CH 1 Agrin ; 1 Integrins ; 1 Laminin ; 1 Receptors, Cholinergic ; 1 integrin alpha7beta1 ; 1 Laminin 1
- 149 ANSWER 16 OF 48 MEDLINE
 AN 01101287648 MEDLINE
 IN 011012848 PubMed ID: 10772822

- TI Laminin alpha4 and **integrin** alpha6 are upregulated in regenerating dy/dy skeletal muscle: comparative expression of laminin and **integrin** isoforms in muscles regenerating after crush injury.
- AC Sorokin L M; Maier M A; Moch H; von der Mark H; von der Mark H; Radlert L; Parosi S; Davies M J; McGeachie J K; Grounds M D
- CS Interdisciplinary Center for Clinical Research - IZKF, University of Erlangen-Nuremberg, Germany.
- SO EXPERIMENTAL CELL RESEARCH, 2000 May 15; 256: 817-14. Journal code: 0378228. ISSN: 0014-4827.
- CV United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200005
- ED Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000518
- AB The expression of laminin isoforms and laminin-binding **integrin** receptors known to occur in muscle was investigated during myogenic regeneration after crush injury. Comparisons were made between dystrophic 109FeJ dy/dy mice, which have reduced laminin alpha2 expression, and their normal littermates. The overall histological pattern of regeneration after crush injury was similar in dy/dy and control muscle, but proceeded faster in dy/dy mice. In vitro studies revealed a greater yield of mononuclear cells extracted from dy/dy muscle and a reduced proportion of desmin-positive cells upon in vitro cultivation, reflecting the presence of inflammatory cells and "preactivated" myoblasts due to ongoing regenerative processes within the endogenous dystrophic lesions. Laminin alpha1 was not detectable in skeletal muscle. Laminin alpha2 was present in basement membranes of mature myofibers and newly formed myotubes in control and dy/dy muscles, albeit weaker in dy/dy. Laminin alpha2-negative myogenic cells were detected in dy/dy and control muscle, suggesting the involvement of other laminin alpha chains in early myogenic differentiation, such as laminin alpha4 and alpha5 which were both transiently expressed in basement membranes of newly formed myotubes of dy/dy and control mice. **Integrin beta1** was expressed on endothelial cells, muscle fibers, and peripheral nerves in uninjured muscle and broadened after crush injury to the interstitium where it occurred on myogenic and nonmyogenic cells. **Integrin** alpha3 was not expressed in uninjured or regenerating muscle, while **integrin** alpha6 was expressed mainly on endothelial cells and peripheral nerves in uninjured muscle. Upon crush injury **integrin** alpha6 increased in the interstitium mainly on nonmyogenic cells, including infiltrating leukocytes, endothelial cells, and fibroblasts. In dy/dy muscle, **integrin** alpha6 occurred on some newly formed myotubes. **Integrin** alpha7 was expressed on muscle fibers at the myotendinous junction and showed weak and irregular expression on muscle fibers. After crush injury, **integrin** alpha7 expression extended to the newly formed myotubes and some myoblasts. However, many myoblasts and newly formed myotubes were **integrin** alpha7 negative. No marked difference was observed in **integrin** alpha7 expression between dy/dy and control muscle, either uninjured or after crush injury. Only laminin alpha4 and **integrin** alpha6 expression patterns were notably different between dy/dy and control muscle. Expression of both molecules was more extensive in dy/dy muscle, especially in the interstitium of regenerating areas and on newly formed myotubes. In view of the faster myogenic regeneration observed in dy/dy mice, the data suggest that laminin alpha4 and **integrin** alpha6 support myogenic regeneration. However, whether these accelerated myogenic effects are a direct consequence of the reduced laminin alpha4 expression in dy/dy mice, or an accentuation of the ongoing regenerative events in focal lesions in the muscle, requires further investigation.

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Check Tags: Animal; Support, Non-U.S. Gov't

*Antigens, CD: ME, metabolism

Fluorescent Antibody Technique

Immunoenzyme Techniques

Integrin alpha3beta1

Integrin alpha6

Integrin alpha6beta1

Integrins: ME, metabolism

*Laminin: ME, metabolism

Mice

Muscle, Skeletal: IN, injuries

*Muscle, Skeletal: ME, metabolism

Muscle, Skeletal: PH, physiology

Protein Isoforms: ME, metabolism

*Regeneration

Up-Regulation

RN 151186-83-2 (Laminin A)

CN * (Antigens, CD); 0 (Integrin alpha3beta1); 0 (Integrin alpha6); 0 (Integrin alpha6beta1); 0 (Integrins); 0 (Laminin); 0 (Protein Isoforms); 0 (integrin alpha7beta1); 0 (Laminin alpha 2); 0 (Laminin alpha 4); 0 (Laminin alpha5)

L83 ANSWER 17 OF 45 MEDLINE

AN 2000175149 MEDLINE

DN 20175149 PubMed ID: 10711985

TI The childhood **muscular dystrophies**: making order out of chaos.

AU Tsao C Y; Mengell J F

CS Department of Neurology, The Ohio State University, Columbus 43210, USA.

SO SEMINARS IN NEUROLOGY, (1999) 19 (1) 9-23. Ref: 145

Journal code: 8111343. ISSN: 0271-8235.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200003

ED Entered STN: 20000413

Last Updated on STN: 20000413

Entered Medline: 20000331

AB New discoveries have dramatically changed the way we approach and think about patients with childhood **muscular dystrophies**. An aura of order and organization seems to be at hand for a group of diseases which previously seemed endlessly heterogeneous. We have learned that young boys and girls with proximal muscle weakness, large calves and elevated serum CK may have any one of a number of closely connected disorders which affect a complex of interacting proteins of the dystrophin-glycoprotein complex. This complex links the intracellular cytoskeleton to the extracellular matrix. Patients with Duchenne and Becker dystrophies lack dystrophin, while some of the limb girdle **muscular dystrophies** (an archaic term) are deficient in sarcoglycans and other proteins. The concept of interrelated disorders extends to the previously orphaned distal **muscular dystrophies**, or distal myopathies, as they are often called. A surprise finding is that the *C. elegans* protein, dysferlin, is conserved and expressed in man. We know little of the function of this protein in human primates, but its loss in muscle has brought seemingly disparate disorders together, since both a form of LMN1 (B) and distal myopathy Miyoshi myopathy are deficient in this same gene product. The congenital **muscular dystrophies** are also well-entrenched in our expanding concepts of orderliness of disease. The

defect in the laminin-alpha chain, a direct ligand to the dystrophin-glycoprotein complex, causes a form of **muscular dystrophy** which affects infants. Another variant of congenital **muscular dystrophy** is deficient the **integrin alpha7**, an important laminin receptor. Finally, in Fukuyama congenital **muscular dystrophy**, the deficient fukutin gene product may also be linked to the basal lamina, permitting overmigration of neuronal cells which lead to micropolygyria in the brain, and at the same time cause basal lamina defects in the extracellular matrix of skeletal muscle, which leads to **muscular dystrophy**. As we approach the millennium, those of us who have seen the transition from the pre-molecular to the molecular era of myology know that we leave behind a great legacy of chaos (no great loss), replaced by a foundation for conceptual organization which will serve to establish new roots for research as well as for the enriched practice of medicine. The future looks bright for our field and our patients!

CT Check Tags: Human

Child

Creatine Kinase: BL, blood

Dystrophin: DF, deficiency

Dystrophin: GE, genetics

*Extracellular Matrix Proteins: GE, genetics

Gene Expression Regulation

Gene Therapy

Laminin: IF, deficiency

Laminin: GE, genetics

*Membrane Glycoproteins: GE, genetics

Muscle Contraction

Muscular Dystrophies: CN, congenital

Muscular Dystrophies: GE, genetics

*Muscular Dystrophies: ME, metabolism

Muscular Dystrophies: PP, physiopathology

Muscular Dystrophies: TH, therapy

Proteins: GE, genetics

Proteins: ME, metabolism

Receptors, Laminin: GE, genetics

CN 0 (Dystrophin); 0 (Extracellular Matrix Proteins); 0 (Laminin); 0 (Membrane Glycoproteins); 0 (Proteins); 0 (Receptors, Laminin); 0 (fukutin); EC 2.7.3.2 (Creatine Kinase)

L83 ANSWER 18 OF 45 MEDLINE

AN 2000160722 MEDLINE

DN 20160722 PubMed ID: 10694445

TI The role of extracellular and cytoplasmic splice domains of **alpha7-integrin** in cell adhesion and migration on laminins.

AC Schober S; Mielenz D; Echtermeyer F; Hapke S; Poschl E; von der Mark H; Moen H; von der Mark K

CS Institute of Experimental Medicine, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, 91054, Germany.

JO EXPERIMENTAL CELL RESEARCH, 1999 Mar 15; 255 (1): 303-13. Journal code: 03782226. ISSN: 0014-4827.

TY United States

JO Journal; Article; JOURNAL ARTICLE

LA English

PC Priority Journals

EM 1999

ED Entered STM: 20000515

Last Updated on STM: 20000515

Entered Medline: 20000424

AB The major laminin-binding **integrin** of skeletal, smooth, and heart muscle is **alpha7beta1-integrin**, which is structurally related to **alpha5beta1**. It occurs in three cytoplasmic splice variants **alpha7A**, **-B**, and **-C** and two extracellular

forms X1 and X2 which are developmentally regulated and differentially expressed in skeletal muscle. Previously, we have shown that ectopic expression of the **alpha7beta-integrin** splice variant in nonmotile HEK293 cells specifically induced cell locomotion on laminin-1 but not on fibronectin. To investigate the specificity and the mechanism of the **alpha7-mediated** cell motility, we expressed the three **alpha7-chain** cytoplasmic splice variants, as well as **alpha6A-** and **alpha6B-integrin** subunits in HEK293 cells. Here we show that all three **alpha7** splice variants (containing the X2 domain), as well as **alpha6A** and **alpha6B**, promote cell attachment and stimulate cell motility on laminin-1 and its E8 fragment. Deletion of the cytoplasmic domain (excluding the GPPKR consensus sequence) from **alpha7B** resulted in a loss of the motility-enhancing effect. On laminin-2/4 (merosin), the predominant isoform in mature skeletal muscle, only **alpha7**-expressing cells showed enhanced motility, whereas cells transfected with **alpha6A** and **alpha6B** neither attached nor migrated on laminin-2. Adhesion of **alpha7**-expressing cells to both laminin-1 and laminin-2 was specifically inhibited by a new monoclonal antibody (6A11) specific for **alpha7**. Expression of the two extracellular splice variants **alpha7X1** and **alpha7X2** in HEK293 cells conferred different motilities on laminin isoforms: Whereas **alpha7X2B** promoted cell migration on both laminin-1 and laminin-2, **alpha7X1B** supported motility only on laminin-2 and not on laminin-1, although both X1 and X2 splice variants revealed similar adhesion rates to laminin-1 and -2. Fluorescence-activated cell sorter analysis revealed a dramatic reduction of surface expression of **alpha6-integrin** subunits after **alpha7A** or **-B** transfection; also, surface expression of **alpha1-**, **alpha3-**, and **alpha5-integrins** was significantly reduced. These results demonstrate selective responses of **alpha6-** and **alpha7-integrins** and of the **alpha7** splice variants to laminin-1 and -2 and indicate differential roles in laminin-controlled cell adhesion and migration. Copyright 2000 Academic Press.

CT Check Tags: Human; Support, Non-U.S. Gov't

*Antigens, CD

Antigens, CD: GE, genetics

Cell Adhesion: GE, genetics

Cell Line

*Cell Movement

Cell Movement: GE, genetics

Integrins: GE, genetics

*Laminin

RNA Splicing

CN 0 Antigens, CD ; 0 (ITGA7 protein, human); 0 (Integrins); 0 (Laminin)

L63 ANSWER 19 OF 45 MEDLINE

AN 2000150162 MEDLINE

DN 20150162 PubMed ID: 10684883

TI Impaired axonal regeneration in **alpha7 integrin**-deficient mice.

AF Werner A; Willem M; Jones L L; Preutzborg S W; Meyer U; Falvick S

TS Department of Neuroanatomy, Max-Planck-Institute of Neurobiology, 81551 Martinsried, Germany.

J JOURNAL OF NEUROSCIENCE, 2001 Mar 1; 21(6): 1822-31.

Journal code: 01621460. ISSN: 1522-2401.

NY United States

SI Journal; Article; JOURNAL ARTICLE

LA English

PS Priority Journals

EM 200003

ED Entered DTN: 20000321

Last Updated on DTN: 20001601

Entered Medline: 20001313

AB The interplay between growing axons and the extracellular substrate is pivotal for directing axonal outgrowth during development and regeneration. Here we show an important role for the neuronal cell adhesion molecule **alpha7beta1 integrin** during peripheral nerve regeneration. Axotomy led to a strong increase of this **integrin** on regenerating motor and sensory neurons, but not on the normally nonregenerating CNS neurons. **alpha7** and **beta1** subunits were present on the axons and their growth cones in the regenerating facial nerve. Transgenic deletion of the **alpha7** subunit caused a significant reduction of axonal elongation. The associated delay in the reinnervation of the whiskerpad, a peripheral target of the facial motor neurons, points to an important role for this **integrin** in the successful execution of axonal regeneration.

OT Check Tags: Animal; Support, Non-U.S. Gov't
*Antigens, CD: FE, genetics
*Axons: PH, physiology

Axotomy

Facial Nerve: CY, cytology

Facial Nerve: FH, physiology

Facial Nerve Injuries: PP, physiopathology

Gene Expression: PH, physiology

Growth Cones: FH, physiology

Growth Cones: UL, ultrastructure

Mice

Mice, Inbred C57BL

Mice, Knockout

Microscopy, Electron

Motor Neurons: PH, physiology

Motor Neurons: UL, ultrastructure

*Nerve Regeneration: FH, physiology

Neuroglia: FH, physiology

CN 0 (Antigens, CD); 0 (ITGA7 protein, human)

L83 ANSWER 20 OF 45 MEDLINE

AN 2000081945 MEDLINE

DN 20081958 PubMed ID: 10616209

TI Organization of the myotendinous junction is dependent on the presence of **alpha7beta1 integrin**.

AU Miosge N; Klenczár C; Herken R; Willem M; Mayer U

CS Zentrum Anatomie, Abteilung Histologie, Universität Göttingen, Germany..
nmiosge@gwdg.de

SO LABORATORY INVESTIGATION, (1999 Dec) 79 (12): 1591-9.
Journal code: 0376617. ISSN: 0023-6937.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 2000001

EO Entered STN: 20000124

Last Updated on STN: 20000124

Entered Medline: 20000113

AB The laminin receptor **alpha7beta1** is enriched at the myotendinous junctions, and mice with a targeted inactivation of the **alpha7** gene develop a form of **muscular dystrophy** that primarily affects this structure. By ultrastructural analysis of **alpha7**-deficient mice, in comparison with wild-type and mdx mice, we attempted to elucidate the role of **alpha7 integrin** for the integrity and function of the myotendinous junctions. Ultrastructurally, myotendinous junctions of **alpha7**-deficient myofibers lose their interdigitations and the myofilaments retract from the sarcolemmal membrane, whereas the lateral side of the myofibers remains morphologically normal. The basement membrane at the myotendinous

functions in **alpha7** - - mice is significantly broadened, and immunogold-histochemistry has demonstrated that the laminin alpha1 chain is not localized here but, instead, in the matrix of the neighboring tendon. In contrast, mdx mice have normal myotendinous junctions, with a matrix protein pattern also found in wild-type mice, however the lateral sides of the myofibers are severely damaged. These results suggest that the **alpha7beta1 integrin** is a major receptor connecting the muscle cell to the tendon and helps to organize the myotendinous junction, whereas the dystrophin-glycoprotein complex is necessary for the lateral integrity of the muscle cell.

CT Check Tags: Animal; Support, Non-U.S. Gov't

Basement Membrane: UL, ultrastructure

Immunohistochemistry

Integrins: GE, genetics

*Integrins: ME, metabolism

Mice

Mice, Inbred mdx

Mice, Knockout

Microscopy, Electron

Muscle, Skeletal: ME, metabolism

*Muscle, Skeletal: UL, ultrastructure

Tendons: ME, metabolism

*Tendons: UL, ultrastructure

CN 0 (Integrins ;) (integrin alpha7beta1)

L83 ANSWER 21 OF 45 MEDLINE

AN 1999364627 MEDLINE

DN 99364627 PubMed ID: 10437916

TI Expression of the **alpha7beta1** laminin receptor suppresses melanoma growth and metastatic potential.

AU Zicher B L; Chen Y Q; Ramos D M; Waleh N; Kramer R H

CS Department of Stomatology, University of California San Francisco, 94143, USA.

NC DE 11912 (NIDCR)

DE 13479 (NIDCR)

SO CELL GROWTH AND DIFFERENTIATION, (1999 Jul) 10 (7) 479-90.

Journal code: 9100024. ISSN: 1044-9523.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199901

ED Entered STN: 19990925

Last Updated on STN: 20000303

Entered Medline: 19990914

AB The **alpha7beta1 integrin** is a laminin-binding receptor

that was originally identified in melanoma. Here, we show that, in clonally derived mouse K1735 melanoma variant cell lines with high (M-2) and low (C-23) metastatic potential, elevated expression of **alpha7** correlates with reduced cell motility, metastasis, and tumor growth. Both cell lines showed similar **beta1 integrin**-dependent adhesion to laminin-1 and the E8 laminin fragment. However, the highly metastatic M-2 cells rapidly migrated on laminin, whereas the nonmetastatic C-23 cells were minimally motile. Laminin-binding **integrin** profiles showed that the M-2 cells expressed moderate amounts of alpha1 and abundant alpha2 but low or undetectable levels of alpha3 and **alpha7**. By contrast, C-23 cells expressed low or undetectable levels of alpha1, alpha2, and alpha3 but had up-regulated levels of **alpha7**. Consistent with the protein data, Northern blot analysis showed that levels of **alpha7** mRNA were highest in the poorly metastatic variant cells, whereas alpha3 message was not detected; in contrast, alpha3 mRNA was elevated in the highly metastatic cells, whereas **alpha7** message was not detected. Forced

expression of **alpha7** in the M-1 cells suppressed cell motility, tumor growth, and metastasis. Collectively, these results indicate that, during melanoma progression, acquisition of a highly tumorigenic and metastatic melanoma phenotype is associated with loss of the **alpha7beta1** laminin receptor.

BT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Adhesion
Cell Movement

Integrins: GE, genetics

*Integrins: ME, metabolism

Laminin: ME, metabolism

Melanoma, Experimental: GE, genetics

Melanoma, Experimental: ME, metabolism

*Melanoma, Experimental: PA, pathology

Mice

Mice, Inbred C3H

Mice, Nude

Neoplasm Metastasis

Neoplasm Transplantation

Receptors, Laminin: GE, genetics

*Receptors, Laminin: ME, metabolism

Transcription, Genetic

Tumor Cells, Cultured

CN 0 (Integrins); 0 (Laminin); 0 (Receptors, Laminin); 0 (integrin **alpha7beta1**)

L83 ANSWER 12 OF 45 MEDLINE

AN 1999097485 MEDLINE

DN 99291485 PubMed ID: 10371075

TI Secondary reduction of **alpha7B integrin** in laminin

alpha2 deficient congenital **muscular dystrophy**

supports an additional transmembrane link in skeletal muscle.

AU Cohn F D; Mayer U; Saher G; Herrmann R; van der Flier A; Sonnenberg A; Stricklin L; Voit T

CS Department of Pediatrics, University of Essen, Germany.

SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (1999 Mar 1) 163 (2) 140-52.

Journal code: 0375403. ISSN: 0022-510X.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199907

ED Entered STN: 19990806

Last Updated on STN: 20020212

Entered Medline: 19990723

AB The **integrins** are a large family of heterodimeric transmembrane cellular receptors which mediate the association between the extracellular matrix (ECM) and cytoskeletal proteins. The **alpha7beta1 integrin** is a major laminin binding **integrin** in skeletal and cardiac muscle and is thought to be involved in myogenic differentiation and migration processes. The main binding partners of the **alpha7 integrin** are laminin-1 **alpha1-beta1** -gamma1, laminin-2 **alpha2-beta1**-gamma1 and laminin-4 **alpha2-beta2**-gamma1. Targeted deletion of the gene for the **alpha7 integrin** subunit "ITGA7" in mice leads to a novel form of **muscular dystrophy**. In the present study we have investigated the expression of two alternative splice variants, the **alpha7B** and **beta15 integrin** subunits, in normal human skeletal muscle, as well as in various forms of **muscular dystrophy**. In normal human skeletal muscle the expression of the **alpha7 integrin** subunit appeared to be developmentally regulated: it was first detected at 3 years of age. In contrast, the **beta15 integrin** could be detected in immature and mature muscle

in the sarcolemma of normal fetal skeletal muscle at 16 weeks gestation. The expression of **alpha7B integrin** was significantly reduced at the sarcolemma in six patients with laminin alpha2 chain deficient congenital **muscular dystrophy** (CMD) age 1-2 years. However, this reduction was not correlated with the amount of laminin alpha2 chain expressed. In contrast, the expression of the laminin alpha2 chain was not altered in the skeletal muscle of the **alpha7** knock-out mice. These data argue in favor that there is not a tight correlation between the expression of the **alpha7 integrin** subunit and that of the laminin alpha2 chain in either human or murine dystrophic muscle. Interestingly, in dystrophinopathies (Duchenne and Becker **muscular dystrophy**; DMD/BMD) expression of **alpha7B** was upregulated irrespective of the level of dystrophin expression as shown by a strong sarcolemmal staining pattern even in young boys (age <2 years). The expression of the beta1D **integrin** subunit was not altered in any of our patients with different types of **muscular dystrophy**. In contrast, sarcolemmal expression of beta1D **integrin** was significantly reduced in the **alpha7 integrin** knock-out mice, whereas the expression of the components of the DGC was not altered. The secondary loss of **alpha7B** in laminin alpha2 chain deficiency defines a biochemical change in the composition of the plasma membrane resulting from a primary protein deficiency in the basal lamina. These findings, in addition to the occurrence of a **muscular dystrophy** in **alpha7** deficient mice, implies that the **alpha7B integrin** is an important laminin receptor within the plasma membrane which plays a significant role in skeletal muscle function and stability.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't

Adolescent

Adult

Aging

Amino Acid Sequence

Antibodies

*Antigens, CD: GE, genetics

Antigens, CD: PE, physiology

Child

Child, Preschool

Cytoskeletal Proteins: GE, genetics

Dystrophin: GE, genetics

Embryo and Fetal Development

Fetus

Gene Expression Regulation, Developmental

Infant

Infant, Newborn

Integrins: GE, genetics

*Laminin: DF, deficiency

*Laminin: GE, genetics

Membrane Glycoproteins: GE, genetics

Mice

Mice, Knockout

Molecular Sequence Data

Muscle Development

Muscle, Skeletal: EM, embryology

Muscle, Skeletal: GE, growth & development

*Muscle, Skeletal: PE, pathophysiology

Muscular Dystrophies: CN, congenital

***Muscular Dystrophies: GE, genetics**

Protein Isoforms: GE, genetics

PK 146888-27-9 48-156K dystrophin-associated glycoprotein

PK 1 Antibodies ; 1 Antigens, CD ; 1 Cytoskeletal Proteins ;

Dystrophin ; 1 ITGA7 protein, human ; 1 **Integrins** ;

Laminin ; 1 Membrane Glycoproteins ; 1 Protein Isoforms ; 1 **Adhesion** ;

Laminin alpha 2

199 ANSWER 23 OF 15 MEDLINE
 AN 19990614 MEDLINE
 DN 99042618 PubMed ID: 10228961
 TI Laminin polymerization induces a receptor-cytoskeleton network.
 AU Colegnato H; Winkelmann D A; Yurchenco P D
 CS Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, USA.
 NO R01-AR38454 (NIAMS)
 R01-DK36425 (NIDDK)
 SO JOURNAL OF CELL BIOLOGY, (1999 May 3) 145 (3) 619-31.
 Journal code: 0378-56. ISSN: 0021-9525.
 CY United States
 DT Journal; Article; [JOURNAL ARTICLE]
 LA English
 FS Priority Journals
 EM 199906
 ED Entered STN: 19990614
 Last Updated in STN: 19990614
 Entered Medline: 19990611
 AB The transition of laminin from a monomeric to a polymerized state is thought to be a crucial step in the development of basement membranes and in the case of skeletal muscle, mutations in laminin can result in severe **muscular dystrophies** with basement membrane defects. We have evaluated laminin polymer and receptor interactions to determine the requirements for laminin assembly on a cell surface and investigated what cellular responses might be mediated by this transition. We found that on muscle cell surfaces, laminins preferentially polymerize while bound to receptors that included dystroglycan and **alpha7beta1 integrin**. These receptor interactions are mediated through laminin COOH-terminal domains that are spatially and functionally distinct from NH2-terminal polymer binding sites. This receptor-facilitated self-assembly drives rearrangement of laminin into a cell-associated polygonal network, a process that also requires actin reorganization and tyrosine phosphorylation. As a result, dystroglycan and **integrin** redistribute into a reciprocal network as do cortical cytoskeleton components vinculin and dystrophin. Cytoskeletal and receptor reorganization is dependent on laminin polymerization and fails in response to receptor occupancy alone (nonpolymerizing laminin). Preferential polymerization of laminin on cell surfaces, and the resulting induction of cortical architecture, is a cooperative process requiring laminin- receptor ligation, receptor-facilitated self-assembly, actin reorganization, and signaling events.
 CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
 Actins: ME, metabolism
 Cells, Cultured
 Cytoskeleton: CH, chemistry
 *Cytoskeleton: ME, metabolism
 *Integrins: ME, metabolism
 *Laminin: CH, chemistry
 *Laminin: ME, metabolism
 Membrane Proteins: CH, chemistry
 Membrane Proteins: ME, metabolism
 Mice
 Mice, Mutant Strains
 Muscle, Skeletal: CY, cytology
 Muscular Dystrophy, Animal: ME, metabolism
 Phosphorylation
 Polymers
 Protein Structure, Tertiary
 Receptors, Laminin: ME, metabolism
 Sarcolemma: CH, chemistry

Sarcolemma: ME, metabolism
 Tyrosine: ME, metabolism
 EN 55117-41-6 (Tyrosine)
 CN 1 A tins ; 1 Integrins ; 1 Laminin ; 1 Membrane Proteins ; 1 Polymers ; 1 Receptors, Laminin ; 1 integrin alpha7beta1 ; 1 Laminin alpha 2

163 ANSWER 24 OF 45 MEDLINE
 AN 1999238963 MEDLINE
 BN 99238963 PubMed ID: 10222457
 TI Merovin-positive congenital **muscular dystrophy**: a large inbred family.
 AU Mahjneh I; Busnby R; Anderson L; Muntoni F; Tolvanen-Mahjneh H; Bashir R; Pinnel A; Brockington M; Marconi G
 CS Department of Neurological and Psychiatric Sciences, University of Florence, Italy.
 SO NEUROPEDIATRICS, (1999 Feb) 30 (1) 22-8.
 Journal code: 31(1987). ISSN: 0174-304X.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199906
 ED Entered STN: 19990623
 Last Updated on STN: 10000303
 Entered Medline: 19990615

AB Large families with congenital **muscular dystrophy** are rare. We report a clinical, histopathological, immunocytochemical, electrophysiological, radiological and genetic study of 10 cases affected by "pure" CMD belonging to two generations of a large inbred Palestinian family. The disease showed autosomal recessive inheritance. All patients had generalised muscular weakness and hypotonia at birth without arthrogryposis. They had a relatively benign clinical course with stabilisation of the clinical picture at different ages and at variable degrees of severity. The pattern of muscle weakness and wasting was more marked in the proximal upper limb-girdle and trunk muscles. Lower limb muscles were more mildly involved. Serum CK was normal or moderately increased. All patients had normal intelligence, normal computed tomography (CT) scans of the brain and normal somatosensory evoked potentials (SEP). Electromyography (EMG) and muscle **biopsy** showed morphological changes compatible with **muscular dystrophy**. Immunocytochemistry for dystrophin, laminin alpha 2 of merosin, and for alpha, beta, gamma sarcoglycans was normal. Linkage analysis excluded all the known loci for CMD, including laminin alpha 2 on chromosome 6q2, the Fukuyama congenital **muscular dystrophy** locus on 9q3, the **integrin alpha 7** locus on chromosome 12q13 and the recently identified locus on 1p35-36. The family we present is clinically and genetically distinct from the already mapped forms of congenital **muscular dystrophy**. Genetic studies are in progress to localise the gene responsible for this condition.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
 Adolescent
 Adult
 Biopsy
 Child
 Child, Preschool
 Chromosome Mapping
 Consanguinity
 Immunohistochemistry
 Infant
 Israel: EH, ethnology
 Laminin: GE, genetics

London

Muscle Hypotonia: ET, etiology

*Muscles: PA, pathology

Muscular Dystrophies: CO, complications

*Muscular Dystrophies: CN, congenital

Muscular Dystrophies: DI, diagnosis

*Muscular Dystrophies: GE, genetics

Pedigree

CN 0 Laminin

L63 ANSWER 25 OF 45 MEDLINE

AN 1999216351 MEDLINE

CN 94216351 PubMed ID: 10199978

TI The **alpha7beta1 integrin** in muscle development and disease.

AU Burkin D J; Kaufman S J

CS Department of Cell and Structural Biology, University of Illinois, B107 Chemical and Life Sciences Laboratory, Urbana, IL 61801, USA.

SO CELL AND TISSUE RESEARCH, (1999 Apr) 296 (1) 183-90. Ref: 43

Journal code: 0417625. ISSN: 0302-766X.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 199905

ED Entered STN: 19990601

Last Updated on STN: 19990601

Entered Medline: 19990517

AB The **alpha7beta1 integrin** is a laminin receptor on the surface of skeletal myoblasts and myofibers. Alternative forms of both the **alpha7** and **beta1** chains are expressed in a developmentally regulated fashion during myogenesis. These different **alpha7beta1** isoforms localize at specific sites on myofibers and appear to have distinct functions in skeletal muscle. These functions include the migration and proliferation of developing myoblasts, the formation and integrity of neuromuscular and myotendinous junctions, and the "gluing" together of muscle fibers that is essential to the generation of contractile force. The **alpha7beta1 integrin** appears to be both directly and indirectly causally related to several muscle diseases. Enhanced expression of **alpha7beta1**-mediated linkage of the extracellular matrix is seen in Duchenne muscular dystrophy and may compensate for the absence of the dystrophin-mediated linkage. Downregulation of expression of the **integrin** may contribute to the development of pathology in congenital laminin deficiencies. Mutations in the **alpha7 integrin** gene underlie additional congenital muscle diseases. The functional roles of this **integrin** in the formation and stability of the neuromuscular and myotendinous junctions and its localization between fibers suggest that altered expression or function of this **integrin** may have widespread involvement in other myopathies. The localization of the **alpha7** gene at human chromosome 11q13 is a useful clue for focusing such studies.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Chromosome Mapping

Chromosomes, Human, Pair 11

Integrins: GE, genetics

*Integrins: PH, physiology

Models, Biological

Muscle Fibers: CY, cytology

*Muscle Fibers: PH, physiology

Muscle, Skeletal: EM, embryology
 *Muscle, Skeletal: EM, physiology
 Muscle, Skeletal: EM, physiopathology
 Neuromuscular Diseases: GE, genetics
 *Neuromuscular Diseases: EM, physiopathology
 Neuromuscular Function: EM, physiology

ON 3 Integrins); 1 integrin alpha7beta1.

183 ANSWER 26 OF 48 MEDLINE
 AN 1999151804 MEDLINE
 DN 99151804 PubMed ID: 10029346
 TI A novel form of familial congenital muscular dystrophy
 in two adolescents.
 AU Salih M A; Al Rayess M; Cutshall S; Urtizberea J A; Al-Turaiki M H; Ozo C
 O; Strano V; Akbar M; Abid M; Andeefani A; Campbell K P
 CS Department of Pediatrics, College of Medicine, King Saud University,
 Riyadh, Saudi Arabia.
 SO NEUROPEDIATRICS, (1998 Dec) 29 (6) 289-93.
 Journal code: 8101197. ISSN: 0174-304X.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199908
 ED Entered STM: 19990807
 Last Updated on STM: 20000303
 Entered Medline: 19990524

AB We report on two brothers (the product of first-degree consanguineous
 marriage; aged 15 and 12 years) who presented with severe hypotonia at
 birth, proximal muscle weakness associated with delayed motor milestones
 but normal cognitive function. Investigations (at 4 years of age)
 revealed mildly elevated serum creatine kinase (CK) levels (300 and 824
 IU/l; N = 210). Muscle **biopsies** showed minimal change
 myopathy, no neurogenic atrophy but remarkable type-1 fibre predominance
 (up to 88.5%) without fibre-type disproportion. Clinical examination at
 12 and 9 years, respectively, showed mild facial weakness and high-arched
 palate in both patients. The younger sibling also had ptosis but
 otherwise normal external ocular muscles. They showed symmetric proximal
 muscle weakness and wasting associated with calf-muscle hypertrophy. They
 could walk independently. A repeat muscle **biopsy** showed
 advanced dystrophic changes in the younger patient at the age of 10 years.
 Virtually all the remaining fibres were type 1. Immunohistochemistry
 revealed normal expression of the dystrophin-glycoprotein complex (DGC),
 including dystrophin, beta-dystroglycan, alpha-(adhalin), beta-, gamma-,
 and delta-sarcoglycan, laminin-alpha2 chain (merosin) and syntrophin.
 Mild dystrophic features and type-1 fibre predominance (92.5%) were seen
 in the **biopsy** of the older patient, whereas immunohistochemistry
 showed normal expression of the DGC. Both cases also showed clear
 expression of **integrin alpha7** at the muscle fibre
 surface and in the blood vessels. Three years later, they could still
 walk, but with difficulty, and the older brother showed enlargement of the
 tongue and echocardiographic features of left ventricular dilated
 cardiomyopathy.

BT Check Tags: Case Report; Human; Male
 Adolescent
 Child
 Child, Preschool
 *Consanguinity
 Disease Progression
 Dystrophin: AN, analysis
 Laminin: AN, analysis
 Muscle, Skeletal: EM, chemistry
 Muscle, Skeletal: EM, pathology

*Muscular Dystrophies: CN, congenital

Muscular Dystrophies: GE, genetics

Muscular Dystrophies: PA, pathology

Ventricular Dysfunction, Left: ET, etiology

CN 0 (Dystrophin); 0 (Laminin)

133 ANSWER 27 OF 43 MEDLINE

AN 1999126400 MEDLINE

DN 99126400 PubMed ID: 9925753

TI The muscle-specific laminin receptor **alpha7 beta1 integrin** negatively regulates **alpha5 beta1** fibronectin receptor function.

AU Tomatis D; Echtermayer F; Schober S; Balzac F; Retta S F; Silengo L; Tarone G

CS Dipartimento di Genetica, Biologia e Biochimica, Universita di Torino, Turin, 10126, Italy.

SO EXPERIMENTAL CELL RESEARCH, (1999 Feb 1) 246 (2) 421-32.
Journal code: 03781226. ISSN: 0014-4827.

CY United States

DT Journal; Article; JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199903

ED Entered STN: 19990326

Last Updated on STN: 19990326

Entered Medline: 19990315

AB **alpha7 beta1** is the major **integrin** complex expressed in differentiated muscle cells where it functions as a laminin receptor. In this work we have expressed the **alpha7 integrin** subunit in CHO cells to investigate the functional properties of this receptor. After transfection with **alpha7** CHO cells acquired the ability to adhere and spread on laminin 1 consistent with the laminin receptor activity of the **alpha7 beta1**. **alpha7** transfectants, however, showed a 70% reduction in the ability to adhere to fibronectin and were unable to assemble a fibronectin matrix. The degree of reduction was inversely related to the level of **alpha7** expression. To define the mechanisms underlying this adhesive defect we analyzed surface expression and functional properties of the **alpha5 beta1** fibronectin receptor. Although cell surface expression of **alpha5 beta1** was reduced by a factor of 20-25% in **alpha7** transfectants compared to control untransfected cells, this slight reduction was not sufficient to explain the dramatic reduction in cell adhesion (70%) and matrix assembly (close to 100%). Binding studies showed that the affinity of 125I-fibronectin for its surface receptor was decreased by 80% in **alpha7** transfectants, indicating that the **alpha5 beta1 integrin** is partially inactivated in these cells. Inactivation can be reversed by Mn2+, a cation known to increase **integrin** affinity for their ligands. In fact, incubation of cells with Mn2+ restored fibronectin binding affinity, adhesion to fibronectin, and assembly of fibronectin matrix in **alpha7** transfectants. These data indicate that **alpha7** expression leads to the functional down regulation of **alpha5 beta1 integrin** by decreasing ligand binding affinity and surface expression. In conclusion, the data reported establish the existence of a negative cooperativity between **alpha7** and **alpha5 integrins** that may be important in determining functional regulation of **integrins** during myogenic differentiation. Copyright 1999 Academic Press.

BT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
CHO Cells
Cell Adhesion
Cell Differentiation

Cell Line

Gene Expression

Hamsters

Integrins: GE, genetics

*Integrins: ME, metabolism

Manganese

Models, Biological

Molecular Sequence Data

Muscles: CY, cytology

*Muscles: ME, metabolism

Rabbits

*Receptors, Fibronectin: ME, metabolism

Receptors, Laminin: GE, genetics

*Receptors, Laminin: ME, metabolism

Transfection

RN 7439-96-5 (Manganese)

CN 0 (Integrins); 0 (Receptors, Fibronectin); 0 (Receptors, Laminin); 0 (integrin alpha7beta1); 0 (integrin alpha7beta1)

L83 ANSWER 28 OF 45 MEDLINE

AN 1999034595 MEDLINE

DN 90034595 PubMed ID: 9817762

TI A functional role for specific spliced variants of the **alpha7beta1 integrin** in acetylcholine receptor clustering.

AU Burkin D J; Gu M; Hodges E L; Campanelli J T; Kaufman S J

CS Department of Cell and Structural Biology, University of Illinois, Urbana, Illinois 61801, USA.

SO JOURNAL OF CELL BIOLOGY, (1998 Nov 16) 143 (4) 1067-75.

J. Journal code: 0021-9525. ISSN: 0021-9525.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199912

ED Entered STN: 19990115

Last Updated on STN: 19990115

Entered Medline: 19991221

AB The clustering of acetylcholine receptors (AChR) on skeletal muscle fibers is an early event in the formation of neuromuscular junctions. Recent studies show that laminin as well as agrin can induce AChR clustering. Since the **alpha7beta1 integrin** is a major laminin receptor in skeletal muscle, we determined if this **integrin** participates in laminin and/or agrin-induced AChR clustering. The alternative cytoplasmic domain variants, **alpha7A** and **alpha7B**, and the extracellular spliced forms, **alpha7X1** and **alpha7X2**, were studied for their ability to engage in AChR clustering. Immunofluorescence microscopy of C2C12 myofibers shows that the **alpha7beta1 integrin** colocalizes with laminin-induced AChR clusters and to a much lesser extent with agrin-induced AChR clusters. However, together laminin and agrin promote a synergistic response and all AChR colocalize with the **integrin**. Laminin also induces the physical association of the **integrin** and AChR. High concentrations of anti-**alpha7** antibodies inhibit colocalization of the **integrin** with AChR clusters as well as the enhanced response promoted by both laminin and agrin. Engaging the **integrin** with low concentrations of anti-**alpha7** antibody initiates cluster formation in the absence of agrin or laminin. Whereas both the **alpha7A** and **alpha7B** cytoplasmic domain variants cluster with AChR, only those isoforms containing the **alpha7X2** extracellular domain were active. These results demonstrate that the **alpha7beta1 integrin** has a physiologic role in laminin-induced AChR clustering, that alternative

splicing is integral to this function of the **alpha7** chain, and that laminin, agrin, and the **alpha7beta1 integrin** interact in a common or convergent pathway in the formation of neuromuscular junctions.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Agrin: CH, chemistry
Agrin: PH, physiology

*Alternative Splicing: PH, physiology

Antibodies

Cells, Cultured

Fluorescent Antibody Technique

*Integrins: GE, genetics

Integrins: IM, immunology

Laminin: CH, chemistry

Laminin: PH, physiology

Mice

*Muscle Fibers: CH, chemistry

Muscle Fibers: CY, cytology

Muscle Fibers: PH, physiology

Neuromuscular Junction: CH, chemistry

Neuromuscular Junction: PH, physiology

Precipitin Tests

Receptors, Cholinergic: CH, chemistry

*Receptors, Cholinergic: ME, metabolism

CN (Agrin); 0 (Antibodies); 0 (Integrins); 0 (Laminin); 0 (Receptors, Cholinergic); 0 (integrin alpha7beta1)

L83 ANSWER 19 OF 45 MEDLINE

AN 1998:04188 MEDLINE

DN 96302198 PubMed ID: 9638332

TI Down-regulation of Laminin-binding **integrins** by 1 alpha,25-dihydroxyvitamin D3 in human melanoma cells in vitro.

AU Hansen C M; Madsen M W; Arensbak B; Skak-Nielsen T; Latini S; Binderup L
CS Department of Biochemistry, Leo Pharmaceutical Products, Ballerup, Denmark.

SO CELL ADHESION AND COMMUNICATION, (1998 Mar) 5 (2) 109-20.
Journal code: 0417027. ISSN: 1061-5385.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199809

ED Entered STN: 19981006

Last Updated on STN: 20000303

Entered Medline: 19980923

AB In the present investigation the effect of 1 alpha,25(OH)2D3 on the expression of the **integrin** laminin receptor on the melanoma cell line SK-MEL-28 has been examined. The SK-MEL-28 cells were shown to contain high-affinity receptors for 1 alpha,25(OH)2D3 and cell proliferation was found to be inhibited in a dose-dependent manner in response to the hormone. Using monoclonal antibodies against the alpha 6-sub-unit of the **integrin** laminin receptor, immunocytochemistry demonstrated that exposure of cells to 1 alpha,25(OH)2D3 for 5 days caused a reduced staining intensity. This observation was further confirmed by dot blot analysis, where a dose-dependent decline of alpha 6 expression was obtained after treatment of the cells with 1 alpha,25(OH)2D3 for 5 days. FACS-analysis was performed in order to quantify this decline, and it was found that the level of alpha 6-subunits on the cell surface was reduced by more than 40%. Additional investigations including Northern blot analyses of poly(A)+RNA extracts also showed a dose-dependent reduction of alpha 6 mRNA. Interestingly, the decrease of alpha 6 expression on the surface of SK-MEL-28 melanoma cells was accompanied by a reduced ability of the cells to adhere to an artificial basement membrane.

In conclusion, the present investigation shows that besides having an antiproliferative effect on the SK-MEL-28 melanoma cells, 1 alpha,25(OH)2D3 is also able to inhibit the surface expression of the alpha 6-subunit of the **integrin** laminin receptor. Moreover, the results strongly indicate that 1 alpha,25(OH)2D3 exerts its regulatory effect on the alpha 6-subunit at the **transcriptional** level rather than at the protein level.

CT Check Tags: Human

*Antigens, CD: BI, biosynthesis

*Antigens, CD: GE, genetics

*Antigens, Surface: BI, biosynthesis

*Antigens, Surface: GE, genetics

*Antineoplastic Agents: PD, pharmacology

*Calcitriol: PD, pharmacology

Cell Division: DE, drug effects

*Gene Expression Regulation, Neoplastic: DE, drug effects

*Growth Inhibitors: PD, pharmacology

Integrin alpha6

Integrin alpha6beta1

Integrin alpha6beta4

*Integrins: BI, biosynthesis

Integrins: GE, genetics

*Laminin: ME, metabolism

*Melanocytes: DE, drug effects

Melanocytes: ME, metabolism

*Melanoma: PA, pathology

*Neoplasm Proteins: BI, biosynthesis

Neoplasm Proteins: GE, genetics

RNA, Messenger: BI, biosynthesis

RNA, Neoplasm: BI, biosynthesis

Receptors, Calcitriol: ME, metabolism

*Receptors, Laminin: BI, biosynthesis

Receptors, Laminin: GE, genetics

Tumor Cells, Cultured

*Tumor Stem Cells: DE, drug effects

Tumor Stem Cells: ME, metabolism

RN 32522-06-3 (Calcitriol)

CN 0 (Antigens, CD); 0 (Antigens, Surface); 0 (Antineoplastic Agents); 0 (Growth Inhibitors); 0 (**Integrin alpha6**); 0 (**Integrin alpha6beta1**); 0 (**Integrin alpha6beta4**); 0 (**Integrins**); 0 (Laminin); 0 (Neoplasm Proteins); 0 (RNA, Messenger); 0 (RNA, Neoplasm); 0 (Receptors, Calcitriol); 0 (Receptors, Laminin); 0 (**integrin alpha7beta1**)

LE3 ANSWER 30 OF 45 MEDLINE

AN 1998250181 MEDLINE

DN 98250181 PubMed ID: 9590299

TI Mutations in the **integrin alpha7** gene cause congenital myopathy.

AB Hayashi Y K; Chou F L; Engvall E; Ogawa M; Matsuda O; Hirabayashi S; Yokochi K; Zicker B L; Kramer R H; Kaufman S J; Ogawa E; Goto Y; Nishida T; Tsukahara T; Wang J Z; Hoffman E P; Arahata K

CS Department of Neuromuscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Kodaira, Tokyo, Japan.

NR AS 14032 NIA

PC 29925

SC NATIVE GENETICS, 1998 May 19; 1: 94-7.

Journal code: 9216914. ISSN: 1061-4036.

SY United States

ST Journal; Article; JOURNAL ARTICLE

LA English

FS Priority Journals

CG GENBANK-AF082061; GENBANK-L23423

EM 199808
 ED Entered STN: 19980611
 Last Updated on STN: 19980611
 Entered Medline: 19980829
 AB The basal lamina of muscle fibers plays a crucial role in the development and function of skeletal muscle. An important laminin receptor in muscle is **integrin alpha7beta1D**. **Integrin beta1** is expressed throughout the body, while **integrin alpha7** is more muscle-specific. To address the role of **integrin alpha7** in human muscle disease, we determined **alpha7** protein expression in muscle **biopsies** from 117 patients with unclassified congenital myopathy and congenital **muscular dystrophy** by immunocytochemistry. We found three unrelated patients with **integrin alpha7** deficiency and normal laminin alpha2 chain expression. To determine if any of these three patients had mutations of the **integrin alpha7** gene, **ITGA7**, we cloned and sequenced the full-length human **ITGA7** cDNA, and **screened** the patients for mutations. One patient had splice mutations on both alleles; one causing a 21-bp insertion in the conserved cysteine-rich region, and the other causing a 93-kp deletion. A second patient was a compound heterozygote for the same 93-kp deletion, and had a 1-bp frame-shift deletion on the other allele. A third showed marked deficiency of **ITGA7** mRNA. Clinically, these patients showed congenital myopathy with delayed motor milestones. Our results demonstrate that mutations in **ITGA7** are involved in a form of congenital myopathy.
 CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 *Antigens, CD: GE, genetics
 Base Sequence
 Child
 Child, Preschool
 Cloning, Molecular
 DNA, Complementary
 Infant
 Molecular Sequence Data
 Muscle, Skeletal: ME, metabolism
 *Muscular Diseases: CN, congenital
 *Muscular Diseases: GE, genetics
 *Mutation
 Polymerase Chain Reaction
 RNA, Messenger: GE, genetics
 CN 0 (Antigens, CD); 0 (DNA, Complementary); 0 (ITGA7 protein, human); 0 (RNA, Messenger)
 L83 ANSWER 31 OF 45 MEDLINE
 AN 1498233460 MEDLINE
 DN 96233460 PubMed ID: 9570924
 TI Interaction of **integrin alpha 7 beta** 1 in G2012 myotubes and in solution with laminin.
 AU Zolkiewska A; Thompson W C; Moss J
 CO Pulmonary-Critical Care Medicine Branch, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland 20892-1590, USA.
 JO EXPERIMENTAL CELL RESEARCH, 1998 Apr 15; 247: 1-16-94.
 Journal code: 03782286. ISSN: 0014-4827.
 CY United States
 DT Journal; Article; JOURNAL ARTICLE
 LA English
 FT Priority Journals
 EM 199808
 ED Entered STN: 19980821
 Last Updated on STN: 19980821
 Entered Medline: 19980814

- AB The dimer of **integrin alpha 7** and **beta 1** is a major laminin-binding receptor in skeletal muscle. We studied interactions of **integrin alpha 7 beta 1** with the extracellular matrix protein laminin in solution and in intact cells. **Integrin alpha 7 beta 1** bound to EHS laminin (laminin-1, composed of alpha 1, **beta 1**, and gamma 1 chains), but not to endogenous laminin expressed in C2C12 myotubes. Northern blot analysis demonstrated that C2C12 myotubes synthesized laminin-1 alpha, beta, and gamma subunits mRNAs. C2C12 laminin was, however, immunologically distinct from EHS laminin; it was not recognized by 5D3 anti-laminin-1 monoclonal antibody, whereas 5A2 and LT3 antibodies reacted equally well with C2C12 and EHS laminins. Following deglycosylation of EHS laminin, separation of the subunits by SDS-PAGE, Western blotting, and partial amino acid sequencing of the protein bands, the epitope recognized by 5D3 antibody was localized to the gamma 1 laminin chain. Following binding in vitro, the complex of EHS laminin and **integrin alpha 7 beta 1** was subject to chemical cross-linking. The two proteins did not undergo cross-linking at the cell surface, consistent with the fact that in intact, resting myotubes **integrin alpha 7 beta 1** interacted poorly with EHS laminin, which may reflect a limited accessibility of **integrin alpha 7 beta 1** in the membrane to laminin or an inactive state of the **integrin**.
- CT Check Tags: Animal
Amino Acid Sequence
Antibody Specificity
Detergents
Epitopes: DE, drug effects
Epitopes: IM, immunology
Integrins: GE, genetics
Integrins: IM, immunology
*Integrins: ME, metabolism
Laminin: GE, genetics
Laminin: IM, immunology
*Laminin: PD, pharmacology
Membrane Proteins: IP, isolation & purification
Mice
Molecular Sequence Data
Muscle, Skeletal: CH, chemistry
*Muscle, Skeletal: CY, cytology
*Muscle, Skeletal: ME, metabolism
Protein Binding
RNA, Messenger: AN, analysis
Receptors, Laminin: GE, genetics
Receptors, Laminin: IM, immunology
*Receptors, Laminin: ME, metabolism
Solubility
- CN 0 (Detergents); 0 (Epitopes); 0 (Integrins); 0 (Laminin); 0 (Membrane Proteins); 0 (RNA, Messenger); 0 (Receptors, Laminin); 1 **integrin alpha7beta1**.
- DE ANSWER 02 OF 45 MEDLINE
AN 19910716 MEDLINE
PM 19910716 PubMed ID: 1427236
TI Altered expression of the **alpha7beta1 integrin** in human and murine muscular dystrophies.
AU Hodges E L; Hayashi Y M; Nishida I; Wang W; Arahata F; Kaufman S J
DE Department of Cell and Structural Biology, University of Illinois, Urbana, USA.
NO A814601 NIA
GM-28742 NIDDK

SO JOURNAL OF CELL SCIENCE, 1997 Nov 11; Pt 11: 1673-81.
 Journal code: 00214457. ISSN: 0021-9536.
 SY ENGLAND: United Kingdom.
 ST Journal; Article; [JOURNAL ARTICLE]
 LA English
 PS Priority Journals
 EM 199801
 ED Entered STN: 19980206
 Last Updated on STN: 20000303
 Entered Medline: 19980127
 AB The **alpha7beta1 integrin** is the primary laminin receptor on skeletal myoblasts and adult myofibers. It has distinct functions during muscle development and contributes to muscle structural integrity. We have studied this **integrin** in cases where expression of dystrophin or laminin are compromised. Immunofluorescence demonstrates an increase in **alpha7beta1** in patients with Duchenne **muscular dystrophy** and in mdx mice that lack dystrophin. Analysis of RNA from mdx mice and from patients with Duchenne and Becker **muscular dystrophies** indicates that the increase in the **alpha7beta1 integrin** is regulated at the level of **alpha7** gene **transcription**. In contrast, the levels of **alpha7beta1 integrin** are severely diminished in patients with laminin alpha2 chain congenital dystrophy **muscular dystrophy** and in dy/dy mice that also do not make the alpha2 laminin chain. Analysis of RNA from the hindlimbs of dy/dy mice demonstrated that in the absence of laminin **alpha7** gene **transcription** is inhibited and limited to specific alternatively spliced isoforms. We suggest that the increased expression of **alpha7beta1 integrin** in the absence of dystrophin compensates for the reduced dystrophin-mediated linkage of fibers with the basal lamina and modulates the development of pathology associated with these diseases. The decrease in **alpha7beta1 integrin** and its **transcripts** in the absence of laminin likely contributes to the severe myopathy that results from laminin alpha2 chain deficiency and suggests that laminin-2 regulates expression of the **alpha7 integrin** gene. The role of the **alpha7beta1 integrin** in muscle integrity also suggests that compromised expression of this receptor may underlie as yet undefined myopathies.
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Adult
 Fluorescent Antibody Technique, Indirect
 Immunoblotting
 *Integrins: BI, biosynthesis
 Mice
 *Muscular Dystrophies: ME, metabolism
 *Muscular Dystrophy, Animal: ME, metabolism
 Polymerase Chain Reaction
 CN 0 (Integrins); 0 (integrin alpha7beta1)
 183 ANSWER 33 OF 45 MEDLINE
 AN 1998065331 MEDLINE
 EN 98065331 PubMed ID: 9401799
 TI Light-microscopic study of the beta 1 integrin subunit in human skeletal muscle.
 AU Heub D; Neurorfer B
 DP Department of Neurology, Friedrich Alexander University of Erlangen-Nurnberg, Germany.
 PI CLINICAL NEUROPATHOLOGY, 1997 Nov-Dec 16; 6: 319-27.
 Journal code: 0214401. ISSN: 0702-8021.
 SY GERMANY: Germany, Federal Republic of
 ST Journal; Article; [JOURNAL ARTICLE]
 LA English

PS Priority Journals
 EM 199801
 ED Entered STN: 19980276
 Last Updated on STN: 20000303
 Entered Medline: 19980129
 AB The **beta 1 integrin** subunit is identical with the CD29 antigen, which is found at the surface of leukocytes. **Integrins** are involved in cell-cell and cell-matrix adhesion, mediate neuronal attachment and neurite outgrowth in response to extracellular matrix proteins in cell culture systems. A few analyses of **beta 1 integrin** subunit have been done on developing and regenerating skeletal muscle in animals; but cell culture systems and animal models differ in some respects from human skeletal muscle in situ. The expression of a **beta 1 integrin** subunit variant in human skeletal muscle was reported merely by Western blot analysis. Our present study, performed with immunohistochemical procedures, attempts to demonstrate the expression of the **beta 1 integrin** subunit in developing, normal adult, and diseased human skeletal muscles. The results demonstrated that the **beta 1 integrin** subunit is expressed in developing, normal adult, regenerating, and denervated human skeletal muscle. In developing muscle, the **beta 1 integrin** subunit was observed in muscle cells at least from 12 to 16 weeks of gestation. In **muscular dystrophy** and inflammatory myopathy the **beta 1 integrin** subunit staining occurs in basophilic muscle fibers. Furthermore, the **beta 1 integrin** subunit is expressed in mature fast twitch type 1 fibers, and in denervated myocytes in neurogenic muscular atrophy. In serial sections, the **beta 1 integrin** subunit, N-CAM (neural cell adhesion molecule) and vimentin are expressed in identical muscle fibers. However, in mature fast twitch type 2 fibers the **beta 1 integrin** subunit is expressed exclusively and in neurogenic muscular atrophy vimentin expression is weak. In conclusion, the **beta 1 integrin** subunit, in human skeletal muscles, probably plays a role in the growth morphology and innervation of developing, regenerating, and denervated myocytes. Furthermore, the observation that the **beta 1 integrin** subunit is enriched in mature fast twitch type 2 fibers indicates that the **beta 1 integrin** subunits may play a role in transducing mechanical forces to extracellular matrix proteins.

CT Check Tags: Female; Human; Male
 Adolescent
 Adult
 Aged
 Aged, 80 and over
 *Antigens, CD29: AN, analysis
 Biological Markers
 Biopsy
 Child
 Embryo and Fetal Development: EM, physiology
 Gestational Age
 *Microscopy: MT, methods
 Middle Age
 *Muscle, Skeletal: CH, chemistry
 *Muscle, Skeletal: EM, embryology
 *Muscle, Skeletal: PA, pathology
 *Muscular Atrophy: ME, metabolism
 *Muscular Atrophy: PA, pathology
 *Muscular Diseases: ME, metabolism
 *Muscular Diseases: PA, pathology
 *Muscular Dystrophies: ME, metabolism
 *Muscular Dystrophies: PA, pathology

Neural Cell Adhesion Molecules: AK, analysis
 Regeneration: PH, physiology
 Vimentin: AK, analysis

EN 0 [Antigens, CD28]; 0 [Biological Markers]; 1 [Neural Cell Adhesion Molecules]; 0 [Vimentin]

LEB ANSWER 34 OF 45 MEDLINE
 AK 1998016417 MEDLINE
 EN 99016417 PubMed ID: 9354797

TI Absence of **integrin alpha 7** causes a novel form of **muscular dystrophy**.

AU Mayer U; Saher G; Fassler R; Bornemann A; Echtermeyer F; von der Mark H; Miosge N; Roschl E; von der Mark K

CS Max-Planck-Institute for Biochemistry, Martinsried, Germany..
 Mayer@biochem.mpg.de

SO NATURE GENETICS, (1997 Nov) 17 (3) 318-23.
 Journal code: 9216904. ISSN: 1061-4036.

CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 OS GENBANK-L25423
 EM 199712
 ED Entered STN: 19980103
 Last Updated on STN: 19990129
 Entered Medline: 19971204

AB **Integrin alpha 7 beta 1**
 is a specific cellular receptor for the basement membrane protein laminin-1 (refs 1,2), as well as for the laminin isoforms -2 and -4 (ref. 3). The **alpha 7** subunit is expressed mainly in skeletal and cardiac muscle and has been suggested to be involved in differentiation and migration processes during myogenesis. Three cytoplasmic and two extracellular splice variants that have been described are developmentally regulated and expressed in different sites in the muscle. In adult muscle, the **alpha 7A** and **alpha 7B** subunits are concentrated in myotendinous junctions but can also be detected in neuromuscular junctions and along the sarcolemmal membrane. To study the potential involvement of **alpha 7 integrin**, during myogenesis and its role in muscle integrity and function, we generated a null allele of the **alpha 7** gene (Itga7) in the germline of mice by homologous recombination in embryonic stem (ES) cells. Surprisingly, mice homozygous for the mutation are viable and fertile, indicating that the **alpha 7 beta 1 integrin** is not essential for myogenesis. However, histological analysis of skeletal muscle revealed typical symptoms of a progressive **muscular dystrophy** starting soon after birth, but with a distinct variability in different muscle types. The observed histopathological changes strongly indicate an impairment of function of the myotendinous junctions. These findings demonstrate that **alpha 7 beta 1 integrin** represents an indispensable linkage between the muscle fibre and the extracellular matrix that is independent of the dystrophin-dystroglycan complex-mediated interaction of the cytoskeleton with the muscle basement membrane.

BT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't
 Antigens, CD: GE, genetics
 Antigens, CD: ME, metabolism
 Extremities: PA, pathology
 Flow Cytometry: MT, methods
 Homozygote
 Mice
 Mice, Inbred Strains
 Mice, Inbred mdx

Mice, Transgenic
Molecular Sequence Data
Muscle Fibers: FA, pathology;
Muscle, Skeletal: FA, pathology;
***Muscular Dystrophy, Animal: GE, genetics**
Phagocytosis
Recombination, Genetic
Tenascin: ME, metabolism
Tendons: FA, pathology
CN 0 (Antigens, CD); 0 (ITGA7 protein, human); 0 (Tenascin)
L83 ANSWER 35 OF 45 MEDLINE
AN 1993012902 MEDLINE
DN 96012902 PubMed ID: 9352853
TI Relation between **integrin alpha7Bbeta1** expression in
human intestinal cells and enterocytic differentiation.
AU Esora N; Vachon P H; Herring-Gillam F E; Ferreault N; Beaulieu J F
CS Departement d'anatomie et de biologie cellulaire, Faculte de medecine,
Universite de Sherbrooke, Quebec, Canada.
SO GASTROENTEROLOGY, (1997 Nov) 113 (5) 1510-21.
Journal code: 0074630. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
OS GENBANK-AF034833
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 20010303
Entered Medline: 19971113
AB BACKGROUND & AIMS: Cell-laminin interactions are principally mediated by
specific membrane receptors of the **integrin** family. The
integrin alpha7beta1 is one of them. Its expression in
the intestine has not yet been investigated although it appears to be a
key element in muscle cell differentiation. In this study, the expression
of its three known isoforms has been analyzed in developing and adult
small intestine and in intestinal cell lines. METHODS: The expression of
the **integrin alpha7beta1** was analyzed by indirect
immunofluorescence, Western blotting, immunoprecipitation, and reverse-
transcription polymerase chain reaction. RESULTS: The
alpha7B isoform, but not the **alpha7A** and **C** isoforms, was
detected in intestinal epithelial cells. In vivo, the presence of the
alpha7B subunit was closely paralleled with (1) acquisition of
differentiation characteristics during development and along the
crypt-villus axis in the adult small intestine and (2) loss of enterocytic
functions in the re-differentiated colonic epithelium. In vitro, the
expression of **alpha7B** was also shown to correlate with the
acquisition of enterocytic functions. In Caco-2 cells, the
alpha7Bbeta1 integrin was found transiently up-regulated
at the onset of sucrase-isomaltase expression. CONCLUSIONS: Taken
together, these results suggest that **alpha7Bbeta1** expression is
correlated with human intestinal cell differentiation.
CT Check Tags: Human; Support, Non-U.S. Gov't
Amino Acid Sequence
*Antigens, CD: AN, analysis
*Antigens, CD28: AN, analysis
Caco-2 Cells
Cell Differentiation
*Intestines: CN, chemistry
Intestines: CY, cytology
Molecular Sequence Data
*Receptors, Laminin: AN, analysis
Up-Regulation

DN : Antigens, CD ; Antigens, CD29 ; Integrin protein, human ; Receptors, Laminin

LA: ANSWER 36 OF 48 MEDLINE

AN: 97460015 MEDLINE

DN: 97460015 PubMed ID: 9312189

TI: **Integrins alpha7beta1 in muscle function and survival. Disrupted expression in merosin-deficient congenital muscular dystrophy.**

AF: Vachon P H; Xu H; Liu L; Loechel F; Hayashi Y; Arahata K; Reed J C; Wewer U M; Engvall E

CS: The Burnham Institute, La Jolla Cancer Research Center, La Jolla, California 92037, USA.

SO: JOURNAL OF CLINICAL INVESTIGATION, (1997 Oct 1) 100 (7) 1870-81. Journal code: 7802877. ISSN: 0011-9738.

CY: United States

DT: Journal; Article; [JOURNAL ARTICLE]

LA: English

FS: Abridged Index Medicus Journals; Priority Journals

EM: 199710

ED: Entered STN: 19971224

Last Updated on STN: 20000303

Entered Medline: 19971029

AB: Mutations in genes coding for dystrophin, for alpha, beta, gamma, and delta-sarcoglycans, or for the alpha2 chain of the basement membrane component merosin (laminin-2/4) cause various forms of **muscular dystrophy**. Analyses of **integrins** showed an abnormal expression and localization of **alpha7beta1** isoforms in myofibers of merosin-deficient human patients and mice, but not in dystrophin-deficient or sarcoglycan-deficient humans and animals. It was shown previously that skeletal muscle fibers require merosin for survival and function (Vachon, P.H., F. Loechel, H. Xu, U.M. Wewer, and E. Engvall. 1996. J. Cell Biol. 134:1483-1497). Correction of merosin deficiency in vitro through cell transfection with the merosin alpha2 chain restored the normal localization of **alpha7beta1D integrins** as well as myotube survival. Overexpression of the apoptosis-suppressing molecule Bcl-2 also promoted the survival of merosin-deficient myotubes, but did not restore a normal expression of **alpha7beta1D integrins**. Blocking of **beta1 integrins** in normal myotubes induced apoptosis and severely reduced their survival. These findings (a) identify **alpha7beta1D integrins** as the de facto receptors for merosin in skeletal muscle; (b) indicate a merosin dependence for the accurate expression and membrane localization of **alpha7beta1D integrins** in myofibers; (c) provide a molecular basis for the critical role of merosin in myofiber survival; and (d) add new insights to the pathogenesis of neuromuscular disorders.

CT: Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Antigens, CD29: ME, metabolism

Cell Differentiation

Cell Survival

Cytoskeletal Proteins: BI, biosynthesis

Dystrophin: DF, deficiency

Dystrophin: GE, genetics

Hamsters

Immunohistochemistry

*Integrins: BI, biosynthesis

Laminin: DF, deficiency

Laminin: GE, genetics

Membrane Glycoproteins: BI, biosynthesis

Mice

Mice, Inbred C57BL

Mice, Inbred mdx
 Mice, Mutant Strains
 *Muscle, Skeletal: PH, physiology
 ***Muscular Dystrophies**: CN, congenital
 Muscular Dystrophy, Animal: CN, congenital
 Receptors, Laminin: BI, biosynthesis
 Sarcolemma: ME, metabolism
 Tissue Distribution
 CN 0 (Antigens, CD29); 0 (Cytoskeletal Proteins); 0 (Dystrophin); 0
 Integrins; 0 (Laminin); 0 (Membrane Glycoproteins); 0 (Receptors,
 Laminin); 0 **integrin alpha7beta1**)
 163 ANSWER 37 OF 45 MEDLINE
 AN 97453329 MEDLINE
 DN 97453329 PubMed ID: 9307969
 TI The laminin-binding activity of the **alpha 7**
 integrin receptor is defined by developmentally regulated splicing
 in the extracellular domain.
 AU Ziober P L; Chen Y; Framer E H
 CS Department of Stomatology, University of California, San Francisco
 94143-0812, USA.
 NC 1E-10306 (NIDCR)
 SO MOLECULAR BIOLOGY OF THE CELL, (1997 Sep; 8 (9) 1723-34.
 Journal code: 9201890. ISSN: 1059-1524.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199711
 ED Entered STN: 19980109
 Last Updated on STN: 20000303
 Entered Medline: 19971204
 AB The expression pattern of the laminin-binding **alpha 7**
 beta 1 integrin is developmentally regulated
 in skeletal, cardiac, and smooth muscle. The X1/X2 alternative splicing
 in the extracellular domain of **alpha 7** is found in the
 variable region between conserved alpha-chain homology repeat domains III
 and IV, a site implicated in ligand binding. To assess differences in
 X1/X2 isoform activity, we generated MCF-7 cell lines transfected with
 alpha 7-X1/X2 cDNAs. Transfectants expressing the
 alpha 7-X2 variant adhered rapidly to laminin 1, whereas
 those expressing **alpha 7-X1** failed to attach. That
 alpha 7-X1 exists in an inactive state was established
 in assays using an activating **beta 1** antibody that
 induced X1-dependent cell adhesion and spreading. Furthermore, the
 activation of **alpha 7-X1** was cell type specific, and
 when expressed in HT1080 cells, the **integrin** was converted into
 a fully functional receptor capable of promoting adhesion. Thus, the
 expression of the **alpha 7-X1/X2 integrin** is
 a novel mechanism that regulates receptor affinity states in a
 cell-specific context and may modulate **integrin**-dependent events
 during muscle development and repair.
 CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
 ***Alternative Splicing**
 Breast Neoplasms
 Carcinoma
 Cell Adhesion: DE, drug effects
 Cell Culture
 Gene Expression Regulation, Developmental
 Integrins: IM, immunology
 ***Integrins**: ME, metabolism
 Isomerism
 *Laminin: ME, metabolism

Ligands
 Manganese: PD, pharmacology
 Protein Binding
 *Receptors, Laminin: ME, metabolism
 Tumor Cells, Cultured
 RN 7439-96-8 (Manganese)
 CN 0 (Integrins); 0 (Laminin); 0 (Ligands); 0 (Receptors, Laminin);
 0 (integrin alpha7beta1)

L83 ANSWER 38 OF 45 MEDLINE
 AN 97428300 MEDLINE
 DN 97428300 PubMed ID: 9281377
 TI The **alpha7beta1 integrin** mediates adhesion and migration of skeletal myoblasts on laminin.
 AU Drawley S; Farrell E M; Wang W; Gu M; Huang H Y; Huynh V; Hodges B L; Dopper D N; Kaufman S J
 CS Center for Neurobiology and Psychiatry, University of California at San Francisco, San Francisco, California 94143-0984, USA.
 NC A514632 (NIA)
 AF41453 (NIAMS)
 GM28341 (NIGMS)
 SO EXPERIMENTAL CELL RESEARCH, (1997 Aug 25) 235 (1) 274-86.
 Journal code: 0378228. ISSN: 0014-4827.
 CY United States
 DT Journal; Article; JOURNAL ARTICLE
 LA English
 FS Priority Journals
 EM 199709
 ED Entered STN: 19971013
 Last Updated on STN: 19971013
 Entered Medline: 19970930
 AB Many aspects of myogenesis are believed to be regulated by myoblast interactions with specific components of the extracellular matrix. For example, laminin has been found to promote adhesion, migration, and proliferation of mammalian myoblasts. Based on affinity chromatography, the **alpha7beta1 integrin** has been presumed to be the major receptor mediating myoblast interactions with laminin. We have prepared a monoclonal antibody, Q26, that specifically reacts with both the X1 and the X2 extracellular splice variants of the **alpha7 integrin** chain. This antibody completely and selectively blocks adhesion and migration of rat L8F63 myoblasts on laminin-1, but not on fibronectin. In contrast, a polyclonal antibody to the fibronectin receptor, **alpha5beta1 integrin**, blocks myoblast adhesion on fibronectin, but not on laminin-1. The **alpha7beta1 integrin** also binds to a mixture of laminin-2 and laminin-4, the major laminin isoforms in developing and adult skeletal muscle, but Q26 is a much less potent inhibitor of myoblast adhesion on the laminin-2/4 mixture than on laminin-1. Based on affinity chromatography, we suggest that this may be due to higher affinity binding of **alpha7X1** to laminin-2/4 than to laminin-1.
 CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Alternative Splicing
 Antibodies, Monoclonal: PD, pharmacology
 Antibody Specificity
 CHO Cells
 Cell Adhesion
 Cell Line
 Cell Movement
 Fibronectins: ME, metabolism
 Hamsters
 Immunoblotting
 Integrins: BI, biosynthesis
 Integrins: IM, immunology

*Integrins: PH, physiology
 Kinetics
 *Laminin: ME, metabolism
 Mice
 Muscle, Skeletal: CN, cytology
 *Muscle, Skeletal: PH, physiology
 Pats
 Receptors, Fibronectin: IM, immunology
 Receptors, Fibronectin: PH, physiology
 *Receptors, Laminin: PH, physiology
 Recombinant Proteins: BI, biosynthesis
 Transfection
 Variation (Genetics)
 CN 0 Antibodies, Monoclonal; 0 (Fibronectins); 0 (Integrins); 0 Laminin; 0 (Receptors, Fibronectin); 0 (Receptors, Laminin); 0 Recombinant Proteins; 0 (integrin alpha7beta1)

L83 ANSWER 39 OF 41 MEDLINE
 AN 97227490 MEDLINE
 DN 97227490 PubMed ID: 9132144
 TI Peripheral nerve involvement in merosin-deficient congenital muscular dystrophy and dy mouse.
 AU Matsumura K; Yamada H; Saito F; Sunada Y; Shimizu T
 CS Department of Neurology and Neuroscience, Teikyo University School of Medicine, Tokyo, Japan.. k-matsu@med.teikyo-u.ac.jp
 SO NEUROMUSCULAR DISORDERS, (1997 Jan) 7 (1) 7-12. Ref: 50
 Journal code: 0111473. ISSN: 0960-8366.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199705
 ED Entered STN: 19970507
 Last Updated on STN: 20000303
 Entered Medline: 19970601

AB Merosin, also called laminin-2, is an isoform of laminin comprised of the alpha 2, beta 1 and gamma 1 chains. Deficiency of merosin alpha 2 chain was recently identified as the primary cause of the classical form of congenital muscular dystrophy (CMD), an autosomal recessive neuromuscular disorder characterised by muscular dystrophy and brain white matter abnormalities. Interestingly, merosin-deficient CMD and its animal model dy mouse are also accompanied by dysmyelination of peripheral motor nerves. In peripheral nerve, merosin is expressed in the endoneurium surrounding the Schwann cell/myelin sheath, while the putative merosin receptors dystroglycan and alpha 6 beta 4 integrin are expressed in the outer membrane of Schwann cell/myelin sheath. Together with the well known fact that the deposition of laminin in the basement membrane is essential for Schwann cell myelination, these findings indicate that the interaction of merosin with dystroglycan and/or alpha 6 beta 4 integrin plays an important role in peripheral myelinogenesis and that the disturbance of this interaction leads to peripheral dysmyelination in merosin deficiency. The clinical significance of peripheral dysmyelination in merosin deficiency is also discussed.
 Check Tags: Animal; Support, Non-U.S. Gov't
 *Laminin: DF, deficiency
 Mice
 *Mice, Mutant Strains: PH, physiology
 Muscular Dystrophies: CN, congenital
 *Muscular Dystrophies: ME, metabolism
 *Muscular Dystrophies: PP, physiopathology

Muscular Dystrophy, Animal: GE, genetics
 *Muscular Dystrophy, Animal: PP, physiopathology
 *Peripheral Nerves: PP, physiopathology
 1 Laminin

DN

193 ANSWER 40 OF 45 MEDLINE

AN 96411781 MEDLINE

DN 96411781 PubMed ID: 8810334

TI **Alpha7 integrin** mediates cell adhesion and migration on specific laminin isoforms.

AU Yao C C; Ziober B L; Squillace R M; Kramer R H

OS Department of Stomatology, Schools of Dentistry and Medicine, University of California San Francisco, 94143-0512, USA.

NC EC1 CA33834 (NCI)

EC1 DB19306 (NIDCR)

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 11) 271 (41) 25598-603.
 Journal code: 295121E. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199611

ED Entered STN: 19961119

Last Updated on STN: 20000303

Entered Medline: 19961119

AB The laminin-binding **alpha7beta1 integrin** receptor is expressed at high levels by skeletal and cardiac muscles and by certain melanocytic cells. We have assessed the potential role of the **alpha7A/B integrin** isoforms in mediating cell adhesion and motility and determined the laminin isoform specificity of this **integrin**. When MCF-7 breast carcinoma cells, normally nonadherent to laminin 1, were stably transfected with cDNA for mouse **alpha7**, they adhered with high efficiency and migrated on laminin 1 substrates. Function-perturbing monoclonal antibodies generated to mouse **alpha7** subunit blocked both adhesion and migration of **alpha7** transfectants on laminin 1 substrates. Additional studies with MCF-7 transfectants revealed that **alpha7beta1** binds well to laminin 1 and to a mixture of laminin 2 and 4 but not to laminin 5. Importantly, **alpha7beta1** was capable of promoting motility on both laminin 1 and laminin 2/4 substrates. However, MCF-7 cells transfected with cDNA for either **alpha7A** or **alpha7B** showed no significant differences in cell adhesion or motility on laminin 1 substrates. Although the role for the alternatively spliced cytoplasmic variants of **alpha7** remains unknown, the results establish that **alpha7beta1** mediates cell adhesive activities on a restricted number of laminin isoforms.

CT Check Tags: Animal; Female; Human; Support, U.S. Gov't, P.H.S.
 Amino Acid Sequence

Antibodies, Monoclonal: PD, pharmacology

Antigens, CD: B1, biosynthesis

Antigens, CD: CH, chemistry

*Antigens, CD: PH, physiology

Base Sequence

Breast Neoplasms

*Cell Adhesion

Cell Line

Cell Movement

DNA Primers

Integrins: PH, physiology

Kinetics

*Laminin

Mice

Molecular Sequence Data

Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism

Transfection

CH 1 (Antibodies, Monoclonal); 1 (Antigens, CD); 1 (cDNA Primers); 1 (ITGA protein, human); 1 (Integrins); 1 (Laminin); 1 (Recombinant Proteins); 1 (integrin alpha7beta1)

183 ANSWER 41 OF 45 MEDLINE

AN 95178218 MEDLINE

CN 95178218 PubMed ID: 7532981

TI Recognition of cryptic sites in human and mouse laminins by rat osteoclasts is mediated by beta 3 and **beta 1 integrins**.

AU Horton M A; Spragg J E; Rodary S C; Helfrich M H

CS I.C.R.F. Haemopoiesis Group, St. Bartholomew's Hospital, London, UK.

SO BJNE, (1994 Nov-Dec) 15 61 639-46.

Journal code: 8004748. ISSN: 8756-3282.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199504

ED Entered STN: 19950419

Last Updated on STN: 19960129

Entered Medline: 19950403

AB Laminins may be encountered by osteoclasts and their precursors in basement membranes when they migrate from periosteal vasculature during skeletal development and in pathological situations. We have examined the recognition by osteoclasts of intact laminins and their proteolytic derivatives, and analysed the mechanism of adhesion. Rat osteoclasts fail to bind intact mouse Engelbreth-Holm-Swarm (EHS) laminin (3% adhesion relative to adhesion to foetal calf serum proteins) and bind only weakly to native human placental laminin (13%) or human merosin (9%). Pepsin treatment of native mouse EHS and human laminins increased osteoclast adhesion. Rat osteoclasts adhered to mouse EHS laminin-derived P1 fragment (70%), but failed to bind the E8 fragment, which contains adhesion sites recognised by some **integrins**. Binding to human and mouse P1 laminins was abolished by treatment with RGD-containing peptides and required divalent cations, but not by YIGSR peptide. Combinations of monoclonal antibodies to rat beta 3 and alpha v **integrins** reduced binding to P1 fragment by 91% and to human laminin by 72%, demonstrating that the major **integrin** involved in rat osteoclast adhesion to proteolysed laminin is alpha v beta 3. Antiserum to **beta 1 integrin** inhibited adhesion to human laminin by 40%, but to P1 fragment by only 8%; this suggests that **beta 1 integrins(s)** contribute to osteoclast adhesion to human laminin but probably not to P1 fragment. The involvement of alpha v beta 3 **integrin** was confirmed using a recombinant human alpha v beta 3 solid phase binding assay, alpha v beta 3 bound to mouse P1 fragment and proteolytically digested human laminin, but not intact laminins. (ABSTRACT TRUNCATED AT 260 WORDS)

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't

Amino Acid Sequence

Antibodies, Monoclonal

Binding, Competitive

Cations, Divalent

Cell Adhesion: IE, drug effects

Integrins: IP, isolation & purification

*Integrins: ME, metabolism

Laminin: CH, chemistry

Laminin: ME, metabolism

Mice

Molecular Sequence Data

Oligopeptides: ME, metabolism
 Osteoclasts: ME, metabolism
 Peptide Fragments: ME, chemistry
 Peptide Fragments: ME, metabolism
 Platelet Glycoprotein GPIIb-IIIa Complex
 Rats
 Receptors, Cytoadhesin: IP, isolation & purification
 Receptors, Cytoadhesin: ME, metabolism
 Receptors, Laminin: ME, metabolism
 Receptors, Vitronectin
 Recombinant Proteins: IP, isolation & purification
 Recombinant Proteins: ME, metabolism
 Snake Venoms: ME, metabolism

RN 11590-64-2 (tyrosyl-isoleucyl-glycyl-seryl-arginine); 99996-88-2
 (arginyl-glycyl-aspartic acid)

CN 0 (Antibodies, Monoclonal); 0 (Cations, Divalent); 0 (Integrins
); 0 (Laminin); 1 (Oligopeptides); 0 (Peptide Fragments); 0 (Platelet
 Glycoprotein GPIIb-IIIa Complex); 0 (Receptors, Cytoadhesin); 0
 (Receptors, Laminin); 0 (Receptors, Vitronectin); 0 (Recombinant
 Proteins); 0 (Snake Venoms); 0 (integrin alpha7beta1)

L83 ANSWER 42 OF 45 MEDLINE
 AN 94230594 MEDLINE
 DN 94230594 PubMed ID: 8175907
 TI Selective modulation of the interaction of **alpha 7**
beta 1 integrin with fibronectin and laminin
 by L-14 lectin during skeletal muscle differentiation.
 AU Gu M; Wang W; Song W K; Cooper D N; Kaufman S J
 CS Department of Cell and Structural Biology, University of Illinois, Urbana
 61801.
 NC GN-18641 (NIGMS)
 SO JOURNAL OF CELL SCIENCE, (1994 Jan) 107 . Pt 1) 175-81.
 Journal code: 0022457. ISSN: 0021-9533.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199406
 ED Entered STN: 19940620
 Last Updated on STN: 19970203
 Entered Medline: 19940605

AB The **alpha 7 beta 1**
integrin was originally identified and isolated from
 differentiating skeletal muscle and shown to be a laminin-binding protein
 (Song et al. (1992) *J. Cell Biol.* 117, 643-657). Expression of the
alpha 7 gene and protein are developmentally regulated
 during skeletal muscle differentiation and have been used to identify
 cells at distinct stages of the myogenic lineage (George-Weinstein et al.
 (1993) *Dev. Biol.* 156, 209-229). The lactoside-binding protein L-14
 exists as a dimer and has been localized on a variety of cells, in
 association with extracellular matrix. During myogenesis *in vitro*, L-14
 is synthesized within replicating myoblasts but it is not secreted until
 these cells commence terminal differentiation and fusion into
 multinucleate fibers (Cooper and Barondes, *J. Cell Biol.* 1991, 117,
 1681-1691). Addition of purified L-14 to myogenic cells plated on laminin
 inhibits myoblast spreading and fusion, suggesting that the L-14 lectin
 regulates muscle cell interactions with the extracellular matrix that are
 germane to myogenic development (Cooper et al. 1991 *J. Cell Biol.* 115,
 1437-1448). We demonstrate here, using affinity chromatography and
 immunoblots, that **alpha 7 beta 1**
 also binds to fibronectin and to the L-14 lectin. L-14 binds to both
 laminin and to the **alpha 7 beta 1**
integrin, and it can effectively inhibit the association of

Laminin and this integrin. Modulation of alpha 7 beta 1 interaction with its ligands by L-14 is selective: L-14 does not bind to fibronectin, nor does it interfere with the binding of fibronectin to alpha 7 beta 1. [ABSTRACT TRUNCATED AT 250 WORDS]

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
 Cell Differentiation
 Cell Line
 Chromatography, Affinity
 Electrophoresis, Polyacrylamide Gel
 *Fibronectins: ME, metabolism
 Galectin 1
 Hemagglutinins: BI, biosynthesis
 *Hemagglutinins: ME, metabolism
 Immunoblotting
 Integrins: IP, isolation & purification
 *Integrins: ME, metabolism
 *Laminin: ME, metabolism
 Molecular Weight
 *Muscles: CY, cytology
 Muscles: ME, metabolism
 Protein Binding
 Rats
 Receptors, Laminin: ME, metabolism
 Recombinant Proteins: IP, isolation & purification
 Recombinant Proteins: ME, metabolism
 Tumor Cells, Cultured

CN 0 (Fibronectins); 0 (Galectin 1); 0 (Hemagglutinins); 0 (Integrins); 0 (Laminin); 0 (Receptors, Laminin); 0 (Recombinant Proteins); 0 (integrin alpha7beta1)

L83 ANSWER 43 OF 45 MEDLINE
 AN 94110297 MEDLINE
 DN 94110297 PubMed ID: 8282763
 TI Alpha 7 beta 1 integrin
 is a component of the myotendinous junction on skeletal muscle.
 AU Bao Z Z; Lakonishok M; Faufman S; Horwitz A F
 CS Department of Biochemistry, University of Illinois at Urbana-Champaign IL 61801.
 NC GM 23244 (NIGMS)
 SO JOURNAL OF CELL SCIENCE, (1995 Oct) 106 (Pt 2) 579-89.
 Journal code: 00224557. ISSN: 0021-9533.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199402
 ED Entered STN: 19940228
 Last Updated on STN: 19940228
 Entered Medline: 19940214

AB Immunization against a 70 kDa band that co-purifies with skeletal muscle integrins has resulted in an antibody directed against the avian alpha 7 integrin subunit. The specificity of the antibody was established by patterns of tissue staining and cross-reactivity with antibodies directed against the cytoplasmic domain of the rat alpha 7 cytoplasmic domain. In sections of adult skeletal muscle the alpha 7 integrin was enriched in the myotendinous junction (MTJ). This localization was unique as neither the alpha 1, alpha 2, alpha 3, alpha 4 and alpha 5 subunit localizes in the myotendinous junction. The distribution of the alpha 7 subunit in the MTJ was examined during embryonic development. alpha 7 expression in the junction is first apparent around embryo day 14 and is almost exclusively at the

developing MTJ at this stage. alpha 5 is expressed with distinctive punctate staining around the junctional area in earlier embryos (11-day). The time of appearance of the **alpha 7** subunit in the MTJ correlates with the insertion of myofibrils into subsarcolemmal densities and folding of the junctional membrane, suggesting a role of the **alpha 7 integrin** in this process. Vinculin is present throughout development of the myotendinous junction, suggesting that the **alpha 7 integrin** recognizes a preformed cytoskeletal structure. The presence of the **alpha 7** subunit in the myotendinous junction and the **alpha 5** subunit in the adhesion plaque demonstrates a molecular difference between these two adherens junctions. It also points to possible origins of junctional specificity on muscle. Differences between these two junctions were developed further using an antibody against phosphotyrosine (PY20). Phosphotyrosine is thought to participate in the organization and stabilization of adhesions. The focal adhesion and the neuromuscular junction, but not the MTJ, contained proteins phosphorylated on tyrosine.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
 Amino Acid Sequence

Antibodies, Monoclonal

Chick Embryo
 Chickens

Fluorescent Antibody Technique

Integrins: GE, genetics

Integrins: IM, immunology

***Integrins: ME, metabolism**

Mice

Molecular Sequence Data

Muscles: EM, embryology

*Muscles: ME, metabolism

Rats

Tendons: EM, embryology

*Tendons: ME, metabolism

Tissue Distribution

CN 3 (Antibodies, Monoclonal); 0 (Integrins); 0 (integrin
 alpha7beta1)

L83 ANSWER 44 OF 45 MEDLINE

AN 93366:24 MEDLINE

DN 93366:24 PubMed ID: 8360188

TI A new isoform of the laminin receptor **integrin alpha 7 beta 1** is developmentally regulated in skeletal muscle.

AC Cello G; Starr L; Quaranta V

CS Department of Cell Biology, Scripps Research Institute, La Jolla, California 92037.

NC CA47853 (NCI)

GM46902 (NIGMS)

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Sep 5) 268 (25): 19019-24.
 Journal code: 2985181R. ISSN: 0021-9258.

JO United States

JO Journal; Article; JOURNAL ARTICLE

LA English

FO Priority Journals

GE GENBANK-116544

EM 123309

ED Entered STM: 12331015

Last Updated on STM: 12331203

Entered Medline: 12331201

AB Within the **integrin** family, there are two groups of receptors that bind laminin. One of these groups comprises the heterodimers **alpha 5 beta 1**, **alpha 6 beta 1**, and **alpha 7 beta 1**, all of which bind

the E1 fragment of laminin, and whose alpha subunits show significant homology at the amino acid sequence level. alpha 3 and alpha 6 exist as isoforms with distinct cytoplasmic domains termed A and B, suggesting that they may couple laminin adhesion to distinct cellular responses. We report the identification of a new alpha 7 mRNA which encodes an alpha 7 protein isoform with an alternative cytoplasmic domain. Based on homology with alpha 3 and alpha 6 isoforms, this new isoform is classified as alpha 7A and the previously published one as alpha 7B. This result extends the similarity between alpha 3, alpha 6, and alpha 7 laminin receptor subunits and suggests a common ancestral gene.

The alpha 7 beta 1 laminin

receptor was proposed to be involved in myogenic differentiation.

However, alpha 7 isoforms were not investigated in

that context. We detected the alpha 7B isoform mRNA

in all tissues and cell types tested, including myocardial and skeletal muscle. In contrast, the alpha 7A isoform was

detectable exclusively in skeletal muscle, not in myocardial muscle or

cells or any other tissues or cell lines tested. Furthermore, the

differentiating skeletal muscle cell line C2C12 expressed only

alpha 7B at the replicating myoblast stage and acquired

alpha 7A expression upon induction of differentiation

and fusion. Splicing of alpha 7B mRNA in C2C12

occurred shortly after myogenin expression and could be an indicator of progression through the program of skeletal muscle differentiation.

CT Check Tags: Animal; Female; Support, U.S. Gov't, P.H.S.

Amino Acid Sequence

Base Sequence

Cell Differentiation

*Gene Expression Regulation

Integrins: CH, chemistry

*Integrins: GE, genetics

Integrins: ME, metabolism

Kinetics

*Laminin: ME, metabolism

Mice

Mice, Inbred BALB C

Mice, Inbred C57BL

Molecular Sequence Data

*Muscle Development

Muscles: CH, chemistry

Muscles: ME, metabolism

Myocardium: CH, chemistry

Myocardium: ME, metabolism

Organ Specificity

Polymerase Chain Reaction

RNA Splicing

RNA, Messenger: AN, analysis

RNA, Messenger: ME, metabolism

CN 0 (Integrins); 0 (Laminin); 0 (RNA, Messenger); 0 (integrin alpha7beta1)

193 ANSWER 48 OF 48 MEDLINE

AN 93139147 MEDLINE

EN 93139147 PubMed ID: 1283164

TI Co-localization and molecular association of dystroglycan with laminin at the surface of mouse and human myotubes.

AN Dickson G; Akad A; Morris G E; Simon H; Noursadeghi M; Walsh F C

CS Department of Experimental Pathology, UMCS, Guy's Hospital, London Bridge, UK.

JO JOURNAL OF CELL SCIENCE, 1992 Dec 15; Pt 4 1229-33.

Journal Code: 0022457. ISSN: 0021-9593.

CV ENGLAND: United Kingdom

JT Journal; Article; JOURNAL ARTICLE
 LA English
 PS Priority Journals
 EM 199312
 ED Entered STN: 19931312
 Last Updated on STN: 19961119
 Entered Medline: 19970224
 AB In Duchenne **muscular dystrophy (DMD)**, deficiency of the protein dystrophin results in necrosis of muscle myofibres, associated with lesions in the sarcolemma and surrounding basal lamina. Dystrophin has been proposed to be a major component of the sub-sarcolemmal cytoskeleton involved in maintaining the integrity of the myofibre plasma membrane, and is known to associate with a group of sarcolemmal glycoproteins, one of which exhibits high affinity binding to the basal lamina component laminin. However, a direct or indirect transmembrane association of dystrophin in muscle cells with the myofibre basal lamina has not been demonstrated. To address this question we have examined dystrophin immunostaining and immunoprecipitation patterns in cultured mouse and human myotubes in comparison with that of the basal lamina component, laminin. Dual-immunolabelling revealed virtually complete co-localization of dystrophin on the inside surface of the muscle cell sarcolemma with plaques and veined arrays of laminin accumulating on the extracellular face. This pattern of laminin and dystrophin distribution was distinct from that of other cell surface molecules expressed in myotubes such as the neural cell adhesion molecule, NCAM, and the **beta 1 integrin** receptor, and immunoprecipitation of dystrophin from solubilized myotube extracts resulted in co-purification of laminin E1 chain confirming an association between these two components. The results thus provide the first direct cellular evidence of a transmembrane linkage between dystrophin in the sarcolemmal cytoskeleton with laminin in the overlying basal lamina. While the immunocytochemical distribution of laminin was apparently normal in dystrophin-deficient muscle cells, elevated levels of soluble laminin were present in extracts of mdx compared with normal mouse skeletal muscle. (ABSTRACT TRUNCATED AT 251 WORDS)
 CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
 Amino Acid Sequence
 Antigens, CD29
 Cell Adhesion Molecules, Neuronal: AN, analysis
 Cells, Cultured
 *Dystrophin: AN, analysis
 Dystrophin: IP, isolation & purification
 Integrins: AN, analysis
 *Laminin: AN, analysis
 Laminin: IP, isolation & purification
 Mice
 Mice, Inbred C57BL: ME, metabolism
 Mice, Mutant Strains
 Microscopy, Fluorescence
 Molecular Sequence Data
 *Muscle Proteins: AN, analysis
 *Muscles: OR, chemistry
 Muscular Dystrophy, Animal: ME, metabolism
 Peptide Fragments: IM, immunology
 *Sarcolemma: OR, chemistry
 CN 1 Antigens, CD29 ; 1 Cell Adhesion Molecules, Neuronal ; 1 Dystrophin ; 1 Integrins ; 1 Laminin ; 1 Muscle Proteins ; 1 Peptide Fragments

= . fil . pix

FILE 'WHIM' ENTERED AT 12:19:16 ON 13 MAY 2013

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FILE LAST UPDATED: 5 MAY 2003 <01030508 UP>
 MOST RECENT DERWENT UPDATE: 20030508 <01030508 UP>
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, TOWERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> SLART (Simultaneous Left and Right Truncation) is now available in the /ABEX field. An additional search field BIX is also provided which comprises both /BI and /ABEX <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d all ateq tech acex 198

L98 ANSWER 1 OF 1 WPIX (D) 2003 THOMSON DERWENT
 AN 2002-674967 [72] WPIX
 DNN N2002-533677 DNO C2002-190172
 TI Identifying individual exhibiting symptoms of **muscular dystrophy**, for diagnosing and treating **muscular dystrophy**, by detecting transcription or translation product of **alpha7beta1 integrin** gene in a tissue sample.
 DC B04 F16 S03
 IN KAUFMAN, S J
 PA (KAUF-1) KAUFMAN S J; (UNII) UNIV ILLINOIS FOUND
 CYC 93
 PI WO 2002066989 A2 20020809 (200272)* EN 53p G01N033-68
 RK: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MX NZ NL OA PT SD SE SI SZ TR TZ U3 ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DE EC EF EG FI GR GD GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LF LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
 US 2001192710 A1 20011219 (200303) G01N033-68
 ADT WO 2002066989 A2 WO 2002-US6376 20020220; US 2002192710 A1 Provisional US 2001-270645P 20010220, Provisional US 2001-286890P 20010427, US 2002-81885 20020220
 PRAI US 2001-286890P 20010427; US 2001-270645P 20010220; US 2002-81885 20020220
 IC ICM 301N033-68; G01N033-68
 IDS A61K148-00; A61P021-00; G12N008-00; G12N015-00; G122001-68
 AB WO 2002066989 A UPAB: 20021119
 NOVELTY - Identifying MI symptoms of **muscular dystrophy** MI in individual suffering from **scapuloperoneal muscular dystrophy** SEMI, comprises detecting a transcription or translation product of an **alpha 7 beta 1 integrin** gene in a tissue sample.
 DETAILED DESCRIPTION - Identifying MI symptoms of **muscular dystrophy** MI in individual suffering from **scapuloperoneal muscular dystrophy** SEMI, comprises detecting a transcription or translation product of an

alpha 7 beta 1 integrin

gene in a tissue sample. (M1) comprises:

- (a) obtaining a tissue sample from an individual exhibiting symptoms of a **dystrophy**, where the sample is obtained from a tissue known in a normal individual to express **alpha 7 beta 1 integrin**;

(b) detecting a transcription or translation product of an **alpha 7 beta 1 integrin** gene in the sample; and

- (c) determining a level of the transcription or translation product of the **alpha 7 beta 1 integrin** gene in the sample as compared with a level in a tissue sample from the same tissue of a normal individual. SFMD is diagnosed when the tissue sample of the individual exhibiting MD symptoms, comprises a level of a transcription or translation product of the **alpha 7 beta 1 integrin** gene in the tissue sample that is lower than the level in a tissue sample from the same tissue of a normal individual.

INDEPENDENT CLAIMS are also included for:

- (1) a reporter gene construct (I) comprising a transcription regulatory sequence of a human **alpha 7 integrin** gene and a reporter coding sequence;

- 2) a recombinant host cell (II) comprising the reporter gene construct;

- 3) identifying (M1) a composition that increases expression of an **alpha 7 integrin** gene, comprises:

- (a) contacting the recombinant host cell with a test composition to produce a contacted recombinant host cell;

- (b) monitoring reporter coding expression in the contacted recombinant host cell and monitoring expression of the reporter coding sequence of the reporter gene construct in a recombinant host cell that has not been contacted with the test composition; and

- (c) determining if the test composition increases reporter coding sequence expression when the expression of the reporter coding sequence is greater in the contacted host cell than in the recombinant host cell that has not been contacted with the test composition, where a composition that increases the expression of an **alpha 7 integrin** gene is identified when the expression of the reporter coding sequence is greater in the contacted host cell than in the recombinant host cell that has not been contacted with the test composition;

- (4) alleviating (M4) symptoms of MD having:

- (a) **alpha 7 integrin** levels that are lower in a patient suffering from or susceptible to MD than in a normal individual, comprises administering to the patient the composition identified by (M3); or

- (b) levels of **alpha 7 integrin**, **dystrophin** and/or **utrophin** that are lower in a patient suffering from or susceptible to MD than in a normal individual, comprises administering to the patient a DNA construct comprising an **alpha 7 integrin** coding sequence operably linked to a transcription regulatory sequence that enables selective expression in muscle cells and a vector sequence.

ACTIVITY - Inotropic.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - (M1-4) are useful for diagnosing, ameliorating and treating **muscular dystrophy** symptoms such as

scapuloperoneal muscular dystrophy or **Duchenne**

muscular dystrophy. The nucleic acid probes, primers or

immunological probes can be used for detecting the reduction of or lack of expression of the **alpha 7 beta 1**

integrin in SFMD.

Dwg. 1111

EC: EPI

EA: DCN

MD EPI: E14-E18; E14-E19; E14-E12; E14-E1201E; E14-E1201E; E11-C17A;
E11-C17EB; E11-C17EB; E11-C17EB; E11-C17EB; E11-K14A; E11-K14E; E11-K14F;
E14-C17E; E14-S13; E14-H14; E14-H14D1; E14-H14E; E14-H14F;
EPI: S13-E14H1; S13-E14H4; S13-E14H6

TECH UPTX: 20021103

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The translation product of an **alpha7beta1 integrin** gene in the tissue sample is detected by contacting the tissue sample using an **alpha7beta1 integrin**-specific antibody that is detectably labeled. A transcription product of an **alpha7beta1 integrin** gene is detected in the tissue sample using reverse transcriptase-polymerase chain reaction (RT-PCR). The primers used in the RT-PCR comprise a sequence of (S4) and (S5). In (M2), where the monitoring and determining steps are carried out in high throughput assay format. In the method of (4), where the MD is Duchenne **muscular dystrophy**. The vector sequence is a virus vector sequence or a plasmid sequence. Administering comprises ex vivo transformation of stem cells or myoblasts isolated from the patient to produce transformed myoblasts and subsequent administration of the transformed stem cell or transformed myoblasts to the patient with the result that the transformed myoblasts differentiate to form muscle cells that express **alpha7 integrin**, where the symptoms of MD is ameliorated.

Preferred Gene Construct: The reporter coding sequence is selected from the group of a green fluorescent protein, luciferase, beta-lactamase, beta-galactosidase, or beta-glucuronidase, or an immunological tag portion. The transcription regulatory sequence comprises a sequence of 1270 base pairs fully defined in the specification. The reporter gene construct further comprises a vector sequence.

Preferred Host Cell: The cell is preferably a cultured muscle cell.

GAACAGCACCTTTCTGGAAG (S4)

CCTTGAACCTGCTGTGCTCT (S5)

ABEX UPTX: 20021103

ADMINISTRATION - Administration may be intravenous, intramuscular or by regional perfusion (all claimed). No dosage details given.

EXAMPLE - No suitable example given.

=> d his

(FILE 'HOME' ENTERED AT 11:24:23 ON 13 MAY 2003)

SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:24:37 ON 13 MAY 2003

E INTEGRIN/CT
11 55 S INTEGRIN (L) (ALPHA7 OR ALPHAVII OR ALPHA7) (7 OR VII) (1) (BETA
E MUSCULAR DYSTROPHY/CT
12 4381 S E3-E18
E E3-ALL
13 6000 S E6,E8
14 7013 S E5,E7/E1
15 7017 S MUSCULAR DYSTROPHY
16 11 S SCAPULOCERONEAL?
17 13 S 11 AND 12-16
18 1 S INTEGRIN L ALPHA7BETAL OR ALPHAVII BETA1 OR ALPHAVII BETA1 OF AL
19 1 S 11 AND 12-16
20 13 S 11,12
21 146 S INTEGRIN L ALPHA 7*
22 32 S INTEGRIN L ALPHA7
23 7169 S INTEGRIN L BETA 1
24 481 S INTEGRIN L BETA1
25 34 S 10-16 AND 111-114
26 18 S 115 AND 111,112 AND 113,114

L17 18 S L16,L18
 E KAUFMAN S AU
 L18 118 S E3,E10
 E KAUFMAN STEPHEN AU
 L19 88 S E3,E7,E8
 L20 1 S E2
 L21 8 S L17 AND L18-L20
 E DIAGNOSIS/CT
 E L17 AND E3+NT
 E DIAGNOSIS/CT
 L22 2 S L17 AND E3+NT
 L23 2 S L17 AND E3-E18
 E E3+ALL
 L24 2 S L17 AND E10+NT

FILE 'HCAPLUS' ENTERED AT 11:36:03 ON 13 MAY 2003

 E ANIMAL TISSUE CT
 E E3+ALL
 L25 15 S L17 AND E3,E4,E2+NT
 E ANIMAL TISSUE CT
 E E22+ALL
 L26 1 S L17 AND E3,E3,E1+NT
 L27 2 S L25,L26 AND L22-L24
 L28 18 S L27,L21-L24,L19-L27
 SEL IN AN 1 8 9
 L29 18 S L27 NOT E1-E7
 L30 18 S L29 AND L1-L29
 L31 18 S L30 AND INTEGRIN?
 L32 18 S L31 AND DYSTROPH?
 L33 1 S L32 AND (DIAGNOS? OR PROGNOS? OR PREDICT?)
 L34 1 S L32 AND SCREEN?
 L35 8 S L33,L34
 L36 11 S L35 NOT L35

FILE 'HCAPLUS' ENTERED AT 11:43:18 ON 13 MAY 2003

FILE 'BIOSIS' ENTERED AT 11:44:04 ON 13 MAY 2003

 E KAUFMAN S AU
 L37 487 S E3,E12
 L38 34 S E43,E48,E41
 L39 11247 S L4 OF L5 OR L6
 L40 68 S L1 OF L8
 L41 13 S L39 AND L40
 L42 1 S L37,L38 AND L39
 L43 16 S L37,L38 AND L40
 L44 4 S L41 AND L42,L43
 L45 13 S L41,L44
 L46 13 S L42,L43 NOT L45
 L47 13 S L45 AND INTEGRIN
 L48 13 S L47 AND (ALPHA?? OR ALPHA ?? OR BETA1 OR BETA 1)
 L49 13 S L46 AND INTEGRIN
 L50 13 S L48 AND (ALPHA?? OR ALPHA ?? OR BETA1 OR BETA 1
 L51 26 S L41-L50

L52 FILE 'HCAPLUS, BIOSIS' ENTERED AT 11:44:58 ON 13 MAY 2003
 29 DUP REM L36 L51 19 DUPLICATES REMOVED

FILE 'HCAPLUS, BIOSIS' ENTERED AT 11:45:42 ON 13 MAY 2003

L53 FILE 'MELLINE' ENTERED AT 11:51:13 ON 13 MAY 2003
 15124 S L4-L11
 E MUSCULAR DYSTROPHY CT
 E E3+ALL

```

L84      10166 S E1-ALL
          S E1-NT
          S MUSCULAR DYSTROPHY CT
          S E1-ALL
L85      2429 S E3-NT
L86      10603 S L83-L85
L87      34 S L1 OR L8
L88      5149 S INTEGRIN AND (ALPHA7? OR ALPHA 7# OR BETA1 OR BETA 1#)
L89      37 S L86 AND L87
L90      33 S L86 AND L88
L91      53 S L89, L91
L92      1 S L91 AND DI/CT
L93      14 S L91 AND E1./CT
          S PROGNOSIS/CT
          S E1-ALL
L94      0 S L91 AND E3-NT
L95      14 S L91, L95
L96      2 S L91 AND SCREEN?
L97      13 S L95, L97
L98      3 S L91 AND ANTIBODIES+NT/CT
L99      4 S L97 AND L98
L99      19 S L97-L99
L71      11 S L91 AND (TRANSCRIPT? OR TRANSLAT?)
L71      16 S L70, L71
L73      16 S L92-L94
L74      17 S L91 NOT L73
L75      16 S L91 AND G8./CT
L76      15 S L75 AND L73
L77      11 S L71 AND L74
L78      16 S L70, L77
L79      37 S L97 AND L91-L75
L80      16 S L99-L78 NOT L79
          SEL IN AN 1 5 10 11 13 14 15 16
L81      8 S L80 AND E1-E24
L81      5 S L73, L91 AND BIOPS?
L83      41 S L79, L91, L82

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FILE 'MEILINE' ENTERED AT 12:03:45 ON 13 MAY 2003

FILE 'WPIX' ENTERED AT 12:03:56 ON 13 MAY 2003

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L84      4 S L1 BIX OF L8/BIX
L84      19 S (P04-H21 OF C04-H21)/MC
L86      27 S L84, L86
L87      3 S L86 AND (ALPHA#BETA1 OR ((ALPHA7# OR ALPHA 7#) AND (BETA1 OR
L88      125 S L4 BIX OR L5/BIX OR L6/BIX
L89      1096 S INTEGRIN/BIX
L90      5 S L86, L90 AND L88
L91      127 S A61P021, IC, ICM, ICS, ICA, ICI AND L86, L89
L92      126 S L91 AND ?DYSTROPH?/BIX
L93      1096 S L84-L86, L93
L94      5 S L88 AND L93
L95      11 S A61P021/IC, ICM, ICS, ICA, ICI AND L91
L96      26 S ?DYSTROPH?/BIX AND L93
L97      34 S L84-L96
          SEL IN AN 5
L98      1 S L97 AND E28-E27
L99      7 S L84 NOT L96

```

FILE 'WPIX' ENTERED AT 12:19:19 ON 13 MAY 2003

FILE 'WPIX' ENTERED AT 12:19:19 ON 13 MAY 2003